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Distinct health burdens associated with social position, work environment and unemployment: a retrospective study in a large population-based French cohort

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ABSTRACT

Objectives: Distinguish the respective effects of social position, work environment and unemployment on cardiovascular and cancer risks.

Design: A retrospective observational study.

Setting: A population-based French cohort (CONSTANCES).

Participants: 130,197 adults enrolled between 2012 and 2021 without missing values.

Primary outcome measures: The associations between social position, work environment and unemployment and the prevalence of cardiovascular events and cancers simultaneously tested with multiple logistic regression models adjusting for common risk factors.

Results: While social position, work environment and unemployment exposure are strongly interrelated with each other, they are not linked to the same cardiovascular and cancer outcomes. Low social position and long unemployment duration are significantly associated with an increased prevalence of angina pectoris, myocardial infarction and peripheral arterial disease (OR=1.22 to 1.90, p<0.04 to <0.0001) but not of stroke. In contrast, bad work environment is associated with an increased prevalence of stroke (OR=1.29, p<0.01) but not of angina pectoris, myocardial infarction and peripheral arterial disease. Low social position is associated with an increased prevalence of cervical and lung cancers (OR=1.73 and 1.95,

p<0.002 and <0.03) and a decreased prevalence of skin cancer (OR=0.70, p<0.0001) while bad work environment is associated with an increased prevalence of breast, skin, prostate and colon cancers (OR=1.31 to 2.91, p<0.0002 to <0.0001). Unemployment exposure is not associated with the prevalence of any type of cancers.

Conclusions: Social position, work environment and unemployment may cumulate their effects during lifetime to further increase cardiovascular and cancer risks and should therefore be considered all together in any preventive strategies.

KEYWORDS

French cohort · retrospective study · social position · work environment · unemployment · cardiovascular event · cancer

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study analyzed recent data collected from a large population-based cohort.

- The respective effects of social position, work environment and unemployment on the prevalence of cardiovascular diseases and cancers were simultaneously tested with multiple logistic regression models adjusting for common confounders.

- Both social position and work environment were globally assessed using a wide array of indicators.

- As the cohort was not totally representative of the general population, the external validity of the findings is not warranted.

- The observational and retrospective nature of the study restricts the possibility of drawing causality.

INTRODUCTION

Social position is a powerful determinant of health, influencing the risk of cardiovascular diseases and cancers in particular.[1–4] The reasons why individuals with low social position usually have higher cardiovascular and cancer risks are many, including material deprivation, limited educational and cultural attainment, easy adoption of unhealthy behaviors, low importance given to the care of one's own health, inability to cope with illness and to access health care. For example, individuals with low social position, as measured by educational level, occupational class or income, are more likely to be exposed to several risk factors such as smoking, alcohol consumption, leisure-time physical inactivity, obesity, diabetes, hypertension, dyslipidemia, depression or sleep disorders.[5–13]

Work environment is another strong determinant of health.[14] Individuals with bad working conditions, as assessed by various physicochemical, biomechanical, organizational or psychosocial indicators, have higher cardiovascular and cancer risks.[15–17] Besides the health effects of bad working conditions, these individuals are also overexposed to common risk factors, including alcohol consumption, smoking, leisure-time physical inactivity, obesity, hypertension, diabetes, depression or sleep disorders.[8, 18–25]

Unemployment can also influence heath, independently from social position and work environment.[26–28] The reasons why unemployed individuals have higher cardiovascular and cancer risks[29–33] remain elusive but overexposure to risk factors, such as alcohol consumption, smoking, leisure-time physical inactivity, unbalanced diet, obesity, diabetes, depression or sleep disorders, is likely involved.[34–40]

Health burdens associated with low social position, bad work environment or unemployment are rarely assessed by taking into account these three conditions simultaneously, yet they are strongly interrelated[8, 41] and often exert their effects in a cumulative way during the lifetime of

individuals. The burden linked to one condition could be explained in part by the confounding of the other conditions. For example, the gradient in the incidence of behavioral risk factors (alcohol consumption, smoking, leisure-time physical inactivity) according to work environment is largely mediated by social position while the social gradient in the incidence of clinical risk factors (obesity, hypertension, dyslipidemia, diabetes, sleep disorders, depression) is rather mediated by work environment.[8]. Another potential issue is that social position and work environment are often characterized by a limited number of indicators, such as educational level, occupational class, income, job strain, night shift or chemical exposure, and are not considered as a whole, which is reality for individuals who are not facing only one or a few social constraints or occupational exposures.

The aim of this retrospective study was to simultaneously assess the relationships between the prevalence of cardiovascular events and cancers, unemployment exposure and global estimates of social position and work environment in a large population-based cohort. Examining whether these interrelated socioeconomic variables are associated to distinct health burdens that could add up during lifetime may be helpful to optimally design preventive strategies.

METHODS

Study population

205,203 adults who were affiliated to the general health insurance system (which covers 85% of the French population) were enrolled in the CONSTANCES cohort between February 2012 and September 2021 using a random sampling scheme stratified on age, sex, socioeconomic status and region.[42] Inclusion criteria comprised the obligation to provide written informed consent, to undergo a comprehensive health examination in one of the twenty-one participating medical centers scattered across metropolitan territory and to complete questionnaires on lifestyle, health-related behaviors, social and occupational conditions. The inclusion rate was rather low (7.3%)[43] in line with those observed in other large population-based cohorts when participants are required to visit a medical center for health-related exams.[44] Note that the authors of the present study did not have access to information that could have identified individual participants during or after data collection. Participants were not involved in the design of this study, nor in its implementation but they will be informed of the results. The cohort received approvals from the Ethics Evaluation Committee of the French National Institute of Health and Medical Research and from the National Committee for the Protection of Privacy and Civil Liberties.

The analyses were performed in a subset of 130,197 participants who had no missing values in all variables that were included in multi-adjusted regression models. The choice of selecting these participants rather than imputing randomly distributed missing data was driven by the fact that the cohort was not representative of the French population due to the low inclusion rate that resulted in the selection of socially privileged people, even though the stratified sampling strategy tried to compensate for the higher non-response rate of individuals with low socioeconomic status.[42] The selection of participants with no missing values only marginally accentuated this bias (supplemental Table 1) and the alternative of using multivariate imputation by chained equations would not have been devoid of other biases.[45]

Social position of participants

Several socioeconomic indicators whose distributions are shown in supplemental Table 2 were considered for assessing social position of participants at inclusion. Educational attainment was classified into four levels depending on the number of years of study: ≤11, 12-13, 14-16 or ≥17. Occupation of participants and spouses was reduced from a ten-level classification in the original inquiry to three grades: blue collar/clerk, intermediate and management. Income that included monthly earnings of all household members was ranked as low (below 1500 euros), middle (between 1500 and 2800 euros), high (between 2800 and 4200 euros) or very high (above 4200 euros). These thresholds were dictated by the inquiry that originally included seven levels of income and the need to balance the number of participants between groups. Social vulnerability was evaluated by a score that was calculated from a questionnaire comprising 11

binary items (Y/N) exploring material and social deprivation:[46] "do you sometimes meet a social worker?", "do you have complementary health insurance?", "do you live as a couple?", "are you a homeowner?", "are there periods in the month when you have real financial difficulties to meet your basic needs?", "have you done any sports activities in the last 12 months?", "have you been to any show over the last 12 months?", "have you been on holiday over the last 12 months?", "have you seen any family member over the last six months?", "if you have difficulties, is there anyone around who could take you in for a few days?", "if you have difficulties, is there anyone around who could provide you with material assistance?". This score was categorized into terciles (low, intermediate or high social vulnerability) for the analyses. Note that participants who were unemployed at inclusion reported the occupation, income and social vulnerability status they had just before the unemployment episode.

Given that these different indicators assess complementary and interdependent aspects of social position (supplemental Figure 1), a global score was calculated by giving for each indicator a value of 1 to the least privileged group, 2 or 3 to intermediary groups and 3 or 4 to the most privileged group, depending if the indicator encompassed 3 or 4 levels, by summing the values and by dividing the sum by the number of available indicators for each participant. This global score was categorized into terciles (low, middle or high social position) for the analyses, as previously reported.[8]

Work environment of participants

A total of 19 occupational exposures whose distributions are shown in supplemental Table 3 were used to characterize work environment of participants at inclusion. These included a series of organizational, physical, biomechanical, chemical and psychosocial factors such as commuting time, clocking in and out, regular working hours (on daily and weekly basis), long working hours (over 10h per week day), night work, dealing with the public, driving on public

road, repetitive work (imposed by a machine, a procedure or someone), working with a screen, standing work posture, handling heavy loads (over one kilogram), physically demanding work, exposure to vibrations, exposure to noise, outdoor work, working in the cold, working in the heat, exposure to chemicals and the scale assessing effort-reward imbalance of work that was divided into terciles (low, average or high imbalance).[47] Note that participants who were unemployed at inclusion reported the work environment they had just before becoming unemployed.

Work environment was considered as a whole, which is reality for workers who are not facing only one or a few occupational exposures.[48] For that purpose, the exposures that were significantly interrelated with each other (supplemental Figure 2) were combined into a global score that was calculated by giving for each exposure a value of 1 to the least exposed group, 3 to the more exposed group, and 2 to intermediary groups whenever the exposure encompassed 3 levels, by summing the values and by dividing the sum by the number of available exposures for each worker. This global score was categorized into terciles (bad, average or good work environment) for the analyses, as already described.[49]

Unemployment experienced by participants

Unemployment exposure of participants during their lifetime was documented by a questionnaire in which they were asked to report each time they had stopped working for a period of more than six months and why (unemployment, health issue, other reason). The existence of past episodes of unemployment was confirmed for each participant by administrative data from the French national pension system which also provided the total number of unemployed quarters. This number, that was used to estimate the duration of

unemployment experienced by each participant, was arbitrarily categorized into three groups (0, 1-19, 20-148 quarters) for the analyses.

Prevalence of risk factors among participants

Several risk factors commonly found in the population were considered. These included four nonmodifiable factors: sex, age that was divided into terciles (18-39, 40-54, 55-75 years old) and parental histories of cardiovascular event or cancer coded as binary variables (Y/N). Three behavioral factors: smoking coded into three categories (current, former, never), lifetime non-moderate alcohol consumption (more than two or three drinks on the same day in women or men, respectively)[50] classified as rarely (never or less than one time per month), sometimes (two or three times per month) or often (one time or more per week), leisure-time physical inactivity whose inquiry was based on a three item questionnaire asking about regular practice of walking or cycling, practicing a sport or gardening or housekeeping over the past 12 months; each item was noted 0 if the answer was no, 1 if the practice was regular but low (less than 15 minutes for sport, or 2 hours for the two other items, per week), 2 if the practice was regular and higher; the score calculated by summing the three items ranged from 0 (not active at all) to 6 (very active) and was used to characterize leisure-time physical inactivity (participants with a score <2). Six clinical risk factors were also retained: body mass index, hypertension, dyslipidemia (either hypercholesterolemia or hypertriglyceridemia), diabetes, sleep disorders and depression. The inquiry into the presence and the age of onset of hypertension, dyslipidemia, diabetes and sleep disorders, which were coded as binary variables (Y/N), was performed by physicians in the medical centers. Body mass index (BMI) was calculated from measured weight and height and coded into three categories (optimal if BMI <25 kg/m^2, overweight if 25≤ BMI <30 kg/m^2, obesity if BMI ≥30 kg/m^2). Depression was assessed using

the Centre of Epidemiologic Studies Depression scale and defined as a score ≥19 in both sexes.[51]

As the validity of self-reported information, even when collected by physicians, can be questioned, the coherence of the relationships between common risk factors and the prevalence of cardiovascular events and cancers was tested (supplemental Table 4). The fact that most of the expected associations were observed after multi-adjustment was a good indication that the collected information was reliable. Notably, the associations of the prevalence of cardiovascular events with sex, age, parental history of cardiovascular event, smoking, hypertension, dyslipidemia, sleep disorders, depression and the associations of the prevalence of cancers with sex, age, parental history of cancer, former smoking and sleep disorders. In any case, if a bias was present, it would likely have been under-reporting with rates varying from one disorder to another: 95.2% for diabetes, 80.4% for hypertension, 77.8% for peripheral arterial disease, 72.4% for myocardial infarction, 71.4% for angina pectoris, 54.5% for stroke.[52]

Prevalence of cardiovascular events and cancers among participants

During the visit in the medical centers, physicians inquired about any non-fatal cardiovascular event and cancer that occurred during the lifetime of participants. Four types of cardiovascular events, coded as binary variables (Y/N), were retained for the analyses: stroke, angina pectoris, myocardial infarction and peripheral arterial disease. The information on the occurrence of any type of cancers was collected but only eight based on body location (breast, skin, prostate, cervical, colon, thyroid, lymphoma, lung), coded as binary variables (Y/N), were analyzed separately due to the limited number of cases in the other locations.

Statistical analyses

The characteristics of cohort participants with or without missing values or of individuals randomly selected from the French population were compared by pairs using Cohen's h measure of effect size with the rule of thumb to categorize substantial differences as small ($0.2 \leq h < 0.5$), medium ($0.5 \leq h > 0.8$) or large ($h \geq 0.8$).[53]

The characteristics of participants according to the past occurrence of cardiovascular event or cancer during their lifetime were compared by calculating standardized mean differences (SMD); values > 0.1 being considered as showing significant differences.[54]

The associations between social position, work environment, unemployment duration and the prevalence of cardiovascular events and cancers were tested with multiple logistic regression modeling. Several types of models were used: models 1 were adjusted for sex, age and parental history of cardiovascular event or cancer; models 2 were adjusted for sex, age, parental history of cardiovascular event or cancer, social position, work environment and unemployment duration; models 3 were adjusted for sex, age, parental history of cardiovascular event, social position, work environment, unemployment duration, lifetime non-moderate alcohol consumption, smoking, leisure-time physical inactivity, body mass index, hypertension, dyslipidemia, diabetes, sleep disorders and depression when investigating the prevalence of cardiovascular events, or for sex, age, parental history of cancer, social position, work environment, unemployment duration, lifetime non-moderate alcohol consumption, smoking, body mass index and sleep disorders when investigating the prevalence of cancers.

Residual analyses were performed to assess the fit of the data, assumptions were checked and the potential influence of outliers was examined for all associations.[55] Statistical significance was fixed a priori at two-sided p-value <0.05.

All analyses were performed with the statistical discovery software JMP 17 Pro (SAS, Cary NC) except the calculation of SMD which was done with R software 4.2.2 and "tableone" package 0.13.2.[56]

RESULTS

Interrelationships between low social position, bad work environment and unemployment duration among participants

As shown in Figure 1, social position, work environment and unemployment duration during lifetime were highly correlated, the lower the social position, the worse the work environment and the longest the unemployment duration.

Characteristics of participants according to the occurrence of non-fatal cardiovascular events during lifetime

Compared to participants who never suffered from cardiovascular event, those who did (2340 participants representing 1.8% of the cohort) were more likely to be old men with parental history of cardiovascular event, low social position, bad work environment and long exposure to unemployment (Table 1). They were also overexposed to several risk factors, including lifetime non-moderate alcohol consumption, former smoking, high body mass index, hypertension, dyslipidemia and diabetes.

Table 1: Characteristics of participants who have or have not had a cardiovascular event.

		Cardiovascular event				SMD
		No		Yes		
		n	%	n	%	
-	**All**	127,857	98.2	2340	1.8	-
Sex	**Women**	66,147	51.7	596	25.5	0.560
	Men	61,710	48.3	1744	74.5	
Age (y)	**18-39**	42,048	32.9	87	3.7	1.147
	40-54	43,890	34.3	380	16.3	
	55-75	41,919	32.8	1873	80.0	
Parental history of cardiovascular event	**No**	97,502	76.3	1334	57.0	0.417
	Yes	30,355	23.7	1006	43.0	
Social position	**High**	37,520	29.3	419	17.9	0.384
	Middle	61,212	47.9	1015	43.4	
	Low	29,125	22.8	906	38.7	
Work environment	**Good**	40,354	31.6	386	16.5	0.662
	Average	46,701	36.5	473	20.2	
	Bad	40,802	31.9	1481	63.3	
Unemployment duration (quarters)	**0**	109,461	85.6	1946	83.2	0.162
	1-19	12,507	9.8	195	8.3	
	20-148	5889	4.6	199	8.5	
Lifetime non-moderate alcohol consumption	**Rarely**	18,104	14.2	272	11.6	0.165
	Sometimes	26,826	21.0	373	15.9	
	Often	82,927	64.8	1695	72.5	
Smoking	**Never**	59,425	46.5	704	30.1	0.432
	Former	43,778	34.2	1287	55.0	
	Current	24,654	19.3	349	14.9	
Leisure-time physical inactivity	**No**	116,132	90.8	2120	90.6	0.008
	Yes	11,725	9.2	220	9.4	
Body mass index	**Optimal**	75,836	59.3	793	33.9	0.539
	Overweight	38,037	29.8	1021	43.6	
	Obese	13,984	10.9	526	22.5	
Hypertension	**No**	116,148	90.8	1295	55.3	0.874
	Yes	11,709	9.2	1045	44.7	
Dyslipidemia	**No**	119,939	93.8	1095	46.8	1.200
	Yes	7918	6.2	1245	53.2	
Diabetes	**No**	126,156	98.7	2113	90.3	0.373
	Yes	1701	1.3	227	9.7	
Sleep disorders	**No**	46,997	36.8	784	33.5	0.068
	Yes	80,860	63.2	1556	66.5	
Depression	**No**	109,684	85.8	1967	84.1	0.048
	Yes	18,173	14.2	373	15.9	

The percentages were calculated relatively to the number of participants who have or have not had a cardiovascular event; the differences between the two groups were assessed by computing standardized mean differences (SMD).

Prevalence of non-fatal cardiovascular events among participants according to social position, work environment and unemployment duration.

Low social position was associated with an increased prevalence of cardiovascular events (OR from 1.22 to 1.90) except stroke whose association was non-significant after adjustment for risk factors, work environment and unemployment duration (Table 2).

Bad work environment was only associated with an increased prevalence of stroke (OR=1.29) (Table 2). Associations with angina pectoris, myocardial infraction and peripheral arterial disease were non-significant after adjustment for risk factors, social position and unemployment duration.

After adjustment for risk factors, social position and work environment, long duration of unemployment (20 to 148 quarters) was associated with an increased prevalence of cardiovascular events (OR from 1.46 to 1.70) except stroke whose association was non-significant whatever the adjustment (Table 2).

Table 2: Adjusted odds ratios (95% confidence interval) for the prevalence of non-fatal cardiovascular events in participants at inclusion according to their social position, work environment and unemployment exposure.

		Type of event	n	%	Models 1	p	Models 2	p	Models 3	p
Social position	High	All	419	1.10	1.00		1.00		1.00	
	Middle		1015	1.63	1.41 (1.25-1.58)	<0.0001	1.26 (1.12-1.42)	0.0001	1.13 (1.00-1.27)	0.05
	Low		906	3.02	2.01 (1.78-2.26)	<0.0001	1.63 (1.44-1.86)	<0.0001	1.27 (1.12-1.45)	0.0003
	High	Stroke	195	0.51	1.00		1.00		1.00	
	Middle		395	0.63	1.18 (0.99-1.40)	0.06	1.08 (0.91-1.29)	0.37	1.01 (0.84-1.20)	0.95
	Low		308	1.03	1.57 (1.31-1.89)	<0.0001	1.35 (1.11-1.64)	0.003	1.09 (0.89-1.33)	0.38
	High	Angina pectoris	116	0.31	1.00		1.00		1.00	
	Middle		319	0.51	1.58 (1.27-1.96)	<0.0001	1.43 (1.15-1.78)	0.001	1.27 (1.02-1.59)	0.03
	Low		285	0.95	2.16 (1.74-2.69)	<0.0001	1.78 (1.41-2.25)	<0.0001	1.40 (1.10-1.78)	0.005
	High	Myocardial infarction	143	0.38	1.00		1.00		1.00	
	Middle		352	0.57	1.43 (1.18-1.75)	0.0003	1.28 (1.05-1.57)	0.01	1.11 (0.90-1.36)	0.34
	Low		326	1.09	2.04 (1.67-2.50)	<0.0001	1.65 (1.34-2.05)	<0.0001	1.22 (1.01-1.52)	0.04
	High	Peripheral arterial disease	34	0.09	1.00		1.00		1.00	
	Middle		97	0.16	1.64 (1.11-2.43)	0.01	1.46 (0.98-2.17)	0.06	1.23 (0.82-1.84)	0.31
	Low		128	0.43	3.40 (2.32-4.98)	<0.0001	2.69 (1.79-4.02)	<0.0001	1.90 (1.26-2.86)	0.002
Work environment	Good	All	386	0.95	1.00		1.00		1.00	
	Average		473	1.00	1.03 (0.90-1.18)	0.70	0.95 (0.83-1.09)	0.50	0.93 (0.80-1.07)	0.28
	Bad		1481	3.50	1.88 (1.67-2.11)	<0.0001	1.61 (1.42-1.82)	<0.0001	1.26 (1.10-1.43)	0.0005
	Good	Stroke	182	0.45	1.00		1.00		1.00	
	Average		218	0.46	1.04 (0.86-1.27)	0.66	1.01 (0.83-1.24)	0.90	0.99 (0.81-1.21)	0.93
	Bad		498	1.18	1.68 (1.40-2.01)	<0.0001	1.54 (1.28-1.86)	<0.0001	1.29 (1.06-1.56)	0.01
	Good	Angina pectoris	115	0.28	1.00		1.00		1.00	
	Average		126	0.27	0.90 (0.70-1.16)	0.41	0.81 (0.63-1.05)	0.12	0.80 (0.62-1.04)	0.09
	Bad		479	1.13	1.79 (1.45-2.21)	<0.0001	1.49 (1.19-1.86)	0.0004	1.09 (0.87-1.37)	0.46
	Good	Myocardial infarction	126	0.31	1.00		1.00		1.00	
	Average		164	0.35	1.05 (0.83-1.33)	0.65	0.96 (0.76-1.22)	0.76	0.93 (0.73-1.18)	0.54
	Bad		531	1.26	1.83 (1.49-2.23)	<0.0001	1.54 (1.24-1.90)	<0.0001	1.13 (0.91-1.40)	0.28
	Good	Peripheral arterial disease	38	0.09	1.00		1.00		1.00	
	Average		48	0.10	1.05 (0.69-1.61)	0.81	0.90 (0.58-1.38)	0.62	0.90 (0.58-1.38)	0.62
	Bad		173	0.41	2.16 (1.50-3.10)	<0.0001	1.55 (1.06-2.27)	0.02	1.21 (0.83-1.78)	0.32
Unemployment duration (quarters)	0	All	1946	1.75	1.00		1.00		1.00	
	1-19		195	1.54	1.00 (0.86-1.16)	0.97	0.98 (0.84-1.14)	0.78	0.96 (0.82-1.12)	0.62
	20-148		199	3.27	1.56 (1.34-1.82)	<0.0001	1.40 (1.21-1.64)	<0.0001	1.39 (1.18-1.63)	<0.0001
	0	Stroke	767	0.69	1.00		1.00		1.00	
	1-19		68	0.54	0.82 (0.64-1.06)	0.13	0.81 (0.63-1.04)	0.10	0.80 (0.63-1.04)	0.09
	20-148		63	1.03	1.18 (0.91-1.53)	0.22	1.08 (0.83-1.40)	0.58	1.08 (0.82-1.40)	0.59
	0	Angina pectoris	598	0.54	1.00		1.00		1.00	
	1-19		60	0.47	1.04 (0.80-1.36)	0.77	1.01 (0.78-1.33)	0.91	1.00 (0.76-1.32)	0.98
	20-148		62	1.02	1.61 (1.23-2.10)	0.0004	1.45 (1.11-1.90)	0.006	1.46 (1.11-1.92)	0.007
	0	Myocardial infarction	667	0.60	1.00		1.00		1.00	
	1-19		76	0.60	1.19 (0.94-1.52)	0.15	1.16 (0.91-1.48)	0.23	1.12 (0.88-1.44)	0.35
	20-148		78	1.28	1.89 (1.48-2.40)	<0.0001	1.71 (1.34-2.17)	<0.0001	1.64 (1.28-2.11)	<0.0001
	0	Peripheral arterial disease	204	0.18	1.00		1.00		1.00	
	1-19		25	0.20	1.25 (0.82-1.89)	0.30	1.17 (0.77-1.78)	0.45	1.08 (0.71-1.65)	0.71
	20-148		30	0.49	2.30 (1.56-3.39)	<0.0001	1.91 (1.29-2.82)	0.001	1.70 (1.14-2.53)	0.009

The percentages were calculated relatively to the number of participants for each social position (high=37,939; middle=62,227; low=30,031), work environment (good=40,740; average=47,174; bad=42,283) or unemployment duration (0 quarter=111,407; 1-19 quarters=12,702; 20-148 quarters=6088).

Models 1 included either social position, work environment or unemployment duration and were adjusted for sex, age and parental history of cardiovascular event.

Models 2 included social position, work environment and unemployment duration and were adjusted for sex, age and parental history of cardiovascular event.

Models 3 included social position, work environment and unemployment duration and were adjusted for sex, age, parental history of cardiovascular event, lifetime non-moderate alcohol consumption, smoking, leisure-time physical inactivity, body mass index, hypertension, dyslipidemia, diabetes, sleep disorders and depression.

Characteristics of participants according to the occurrence of non-fatal cancers during lifetime

Compared to participants who never suffered from cancer, those who did (5930 participants representing 4.6% of the cohort) were more likely to be old women with parental history of cancer, low social position, bad work environment and long exposure to unemployment (Table 3). They were also overexposed to risk factors such as former smoking, high body mass index and sleep disorders.

Table 3: Characteristics of participants who have or have not had a cancer.

		Cancer				SMD
		No		Yes		
		n	%	n	%	
-	All	124,267	95.4	5930	4.6	-
Sex	Women	63,160	50.8	3583	60.4	0.118
	Men	61,107	49.2	2347	39.6	
Age (y)	18-39	41,738	33.6	397	6.7	0.920
	40-54	42,905	34.5	1365	23.0	
	55-75	39,624	31.9	4168	70.3	
Parental history of cancer	No	82,462	66.4	3088	52.1	0.282
	Yes	41,805	33.6	2842	47.9	
Social position	High	36,471	29.4	1468	24.7	0.151
	Middle	59,466	47.8	2761	46.6	
	Low	28,330	22.8	1701	28.7	
Work environment	Good	39,356	31.7	1384	23.3	0.441
	Average	45,771	36.8	1403	23.7	
	Bad	39,140	31.5	3143	53.0	
Unemployment duration (quarters)	0	106,389	85.6	5018	84.6	0.088
	1-19	12,170	9.8	532	9.0	
	20-148	5708	4,6	380	6.4	
Lifetime non-moderate alcohol consumption	Rarely	17,503	14.1	873	14.7	0.042
	Sometimes	25,994	20.9	1205	20.3	
	Often	80,770	65.0	3852	65.0	
Smoking	Never	57,498	46.3	2631	44.4	0.240
	Former	42,482	34.2	2583	43.6	
	Current	24,287	19.5	716	12.0	
Body mass index	Optimal	73,501	59.1	3128	52.8	0.165
	Overweight	37,093	29.9	1965	33.1	
	Obese	13,673	11.0	837	14.1	
Sleep disorders	No	45,861	36.9	1920	32.4	0.073
	Yes	78,406	63.1	4010	67.6	

The percentages were calculated relatively to the number of participants who have or have not had a cancer; the differences between the two groups were assessed by computing standardized mean differences (SMD).

Prevalence of non-fatal cancers among participants according to social position, work environment and unemployment duration.

After adjustment for risk factors, work environment and unemployment duration, low social position was not associated with the prevalence of cancers when they were considered globally (Table 4). However, it was directly associated with cervical and lung cancers (OR=1.73 and 1.95 respectively) while it was strongly and inversely associated with skin cancer (OR=0.70).

After adjustment for risk factors, social position and unemployment duration, bad work environment was associated with an increased prevalence of cancers when they were considered globally (OR=1.45) (Table 4). More precisely, it was directly associated with breast, skin, prostate and colon cancers (OR from 1.31 to 2.91).

Unemployment duration was not associated with the prevalence of any type of cancers whatever the adjustment (supplemental Table 5).

Table 4: Adjusted odds ratios (95% confidence interval) for the prevalence of non-fatal cancers in participants at inclusion according to their social position and work environment.

		Body location	n	%	Models 1	p	Models 2	p	Models 3	p
Social position	High	All	1468	3.87	1.00		1.00		1.00	
	Middle		2761	4.44	1.05 (0.98-1.12)	0.16	0.97 (0.91-1.04)	0.47	0.97 (0.91-1.04)	0.44
	Low		1701	5.66	1.12 (1.04-1.21)	0.003	0.98 (0.91-1.06)	0.63	0.98 (0.91-1.07)	0.71
	High	Breast	385	1.01	1.00		1.00		1.00	
	Middle		753	1.21	1.00 (0.88-1.13)	0.99	0.95 (0.84-1.08)	0.44	0.95 (0.83-1.08)	0.42
	Low		452	1.51	1.08 (0.94-1.24)	0.29	0.99 (0.85-1.15)	0.87	0.99 (0.85-1.15)	0.88
	High	Skin	453	1.19	1.00		1.00		1.00	
	Middle		679	1.09	0.85 (0.75-0.96)	0.008	0.81 (0.71-0.92)	0.0008	0.83 (0.73-0.94)	0.003
	Low		333	1.11	0.71 (0.62-0.82)	<0.0001	0.65 (0.56-0.76)	<0.0001	0.70 (0.60-0.81)	<0.0001
	High	Prostate	146	0.38	1.00		1.00		1.00	
	Middle		306	0.49	1.18 (0.96-1.44)	0.11	0.91 (0.74-1.12)	0.38	0.92 (0.75-1.13)	0.44
	Low		232	0.77	1.23 (0.99-1.51)	0.06	0.82 (0.66-1.03)	0.09	0.84 (0.67-1.05)	0.12
	High	Cervical	60	0.16	1.00		1.00		1.00	
	Middle		162	0.26	1.53 (1.13-2.06)	0.005	1.48 (1.09-2.00)	0.01	1.41 (1.04-1.91)	0.03
	Low		103	0.34	2.01 (1.45-2.79)	<0.0001	1.86 (1.32-2.61)	0.0003	1.73 (1.22-2.44)	0.002
	High	Colon	61	0.16	1.00		1.00		1.00	
	Middle		146	0.23	1.29 (0.95-1.74)	0.10	1.12 (0.82-1.52)	0.47	1.12 (0.82-1.52)	0.48
	Low		104	0.35	1.43 (1.04-1.97)	0.03	1.14 (0.82-1.59)	0.44	1.15 (0.82-1.61)	0.42
	High	Thyroid	74	0.20	1.00		1.00		1.00	
	Middle		160	0.26	1.23 (0.93-1.62)	0.14	1.20 (0.91-1.60)	0.19	1.21 (0.91-1.61)	0.18
	Low		91	0.30	1.34 (0.98-1.84)	0.06	1.30 (0.94-1.80)	0.12	1.31 (0.94-1.83)	0.11
	High	Lymphoma	77	0.20	1.00		1.00		1.00	
	Middle		148	0.24	1.15 (0.87-1.51)	0.33	1.14 (0.86-1.52)	0.35	1.13 (0.85-1.50)	0.41
	Low		79	0.26	1.13 (0.82-1.56)	0.44	1.11 (0.79-1.56)	0.55	1.09 (0.77-1.54)	0.63
	High	Lung	13	0.03	1.00		1.00		1.00	
	Middle		32	0.05	1.40 (0.73-2.68)	0.30	1.35 (0.70-2.61)	0.37	1.24 (0.64-2.41)	0.52
	Low		33	0.11	2.36 (1.23-4.52)	0.01	2.23 (1.12-4.42)	0.02	1.95 (1.02-3.90)	0.03
Work environment	Good	All	1384	3.40	1.00		1.00		1.00	
	Average		1403	2.97	0.93 (0.86-1.01)	0.06	0.93 (0.86-1.01)	0.07	0.92 (0.85-1.01)	0.06
	Bad		3143	7.43	1.47 (1.37-1.57)	<0.0001	1.47 (1.37-1.58)	<0.0001	1.45 (1.35-1.56)	<0.0001
	Good	Breast	415	1.02	1.00		1.00		1.00	
	Average		377	0.80	0.93 (0.81-1.07)	0.34	0.93 (0.81-1.08)	0.34	0.92 (0.80-1.06)	0.26
	Bad		798	1.89	1.31 (1.16-1.49)	<0.0001	1.32 (1.16-1.50)	<0.0001	1.31 (1.15-1.49)	<0.0001
	Good	Skin	380	0.93	1.00		1.00		1.00	
	Average		362	0.77	0.86 (0.74-1.01)	0.06	0.90 (0.77-1.04)	0.14	0.91 (0.78-1.05)	0.19
	Bad		723	1.71	1.19 (1.04-1.35)	0.01	1.33 (1.16-1.53)	<0.0001	1.34 (1.16-1.54)	<0.0001
	Good	Prostate	68	0.17	1.00		1.00		1.00	
	Average		52	0.11	0.62 (0.43-1.01)	0.06	0.65 (0.45-1.01)	0.06	0.65 (0.45-1.02)	0.07
	Bad		564	1.33	2.72 (2.11-3.51)	<0.0001	2.90 (2.23-3.79)	<0.0001	2.91 (2.23-3.80)	<0.0001
	Good	Cervical	97	0.24	1.00		1.00		1.00	
	Average		95	0.20	0.97 (0.73-1.29)	0.86	0.93 (0.70-1.24)	0.63	0.92 (0.69-1.22)	0.56
	Bad		133	0.31	1.28 (0.97-1.70)	0.08	1.12 (0.84-1.50)	0.42	1.14 (0.86-1.52)	0.36
	Good	Colon	49	0.12	1.00		1.00		1.00	
	Average		58	0.12	1.08 (0.73-1.58)	0.70	1.06 (0.72-1.55)	0.77	1.05 (0.72-1.54)	0.80
	Bad		204	0.48	2.00 (1.45-2.76)	<0.0001	1.94 (1.39-2.70)	0.0001	1.90 (1.36-2.65)	0.0002
	Good	Thyroid	86	0.21	1.00		1.00		1.00	
	Average		103	0.22	1.14 (0.85-1.51)	0.38	1.11 (0.83-1.48)	0.47	1.09 (0.82-1.46)	0.54
	Bad		136	0.32	1.25 (0.94-1.66)	0.13	1.18 (0.88-1.59)	0.27	1.16 (0.86-1.56)	0.33
	Good	Lymphoma	90	0.22	1.00		1.00		1.00	
	Average		83	0.18	0.79 (0.59-1.07)	0.13	0.78 (0.58-1.06)	0.11	0.77 (0.57-1.04)	0.09
	Bad		131	0.31	1.07 (0.80-1.42)	0.64	1.03 (0.77-1.40)	0.83	1.01 (0.75-1.37)	0.92
	Good	Lung	14	0.03	1.00		1.00		1.00	
	Average		20	0.04	1.24 (0.62-2.46)	0.54	1.12 (0.56-2.24)	0.74	1.07 (0.54-2.15)	0.84
	Bad		44	0.10	1.62 (0.87-3.03)	0.13	1.29 (0.67-2.47)	0.45	1.24 (0.64-2.38)	0.52

The percentages were calculated relatively to the number of participants for each social position (high=37,939; middle=62,227; low=30,031) or work environment (good=40,740; average=47,174; bad=42,283).

Models 1 included either social position, work environment or unemployment duration and were adjusted for sex, age and parental history of cancer.

Models 2 included social position, work environment and unemployment duration and were adjusted for sex, age and parental history of cancer.

Models 3 included social position, work environment and unemployment duration and were adjusted for sex, age, parental history of cancer, lifetime non-moderate alcohol consumption, smoking, body mass index and sleep disorders.

DISCUSSION

The present analyses report the prevalence of cardiovascular events and cancers according to social position, work environment and unemployment exposure in a large population-based French cohort. The retrospective design of the study privileges a holistic approach in which a wide array of indicators is used to globally characterize social position and work environment in order to provide a better assessment of what people face in real life. The results show that social position, work environment and unemployment exposure are strongly interrelated with each other in a way where people are either all good or all bad. The public health issue therefore first arises from people who cumulate a low social position, a bad work environment and a long exposure to unemployment.

The main finding is that, despite their strong interrelationships, social position, work environment and unemployment exposure are not linked to the same cardiovascular and cancerous outcomes. Thus, low social position and long unemployment duration are associated with an increased prevalence of angina pectoris, myocardial infarction and peripheral arterial disease but not of stroke. In contrast, bad work environment is associated with an increased prevalence of stroke but not of angina pectoris, myocardial infarction and peripheral arterial disease. These results add to previously reported data[1, 2, 31] by clearly showing distinct effects of social position and unemployment on one side and work environment on the other side on the risk of cardiovascular events. They also echo the fact that social position and work environment do not predict the incidence of the same risk factors, i.e., mainly behavioral factors (non-moderate alcohol consumption, smoking, leisure-time physical inactivity) for social position, mostly clinical factors (obesity, hypertension, dyslipidemia, diabetes, sleep disorders, depression) for work environment.[8] Overall, these results point out the existence of distinct etiologic mechanisms underlying coronary/peripheral and cerebrovascular diseases with

potentially different risk factors.[57] From a public health viewpoint, considering social position, work environment and unemployment exposure as risk factors remains of little practical interest to prevent cardiovascular events as they are hardly modifiable. However, they can indicate the need for more thorough monitoring of risk factors in people who cumulate low social position, bad work environment and long exposure to unemployment.

A similar conclusion can be drawn from the results showing that social position and work environment are not associated with the same types of cancers. While low social position is associated with an increased prevalence of cervical and lung cancers and a decreased prevalence of skin cancer, bad work environment is associated with an increased prevalence of breast, skin, prostate and colon cancers. These findings add to other studies[58–64] by delimiting in the same cohort the respective effects of social position and work environment on cancer risk. These distinct effects may be mediated by different risk factors such as sleep disorders in the case of bad work environment or smoking in the case of social position.

The finding that unemployment exposure is not associated with the prevalence of any type of cancers is in disagreement with results from previous studies.[29, 32] This discrepancy might arise from the absence of adjustment for work environment in these studies, leaving the possibility that the observed increase in the prevalence of some types of cancers would be related to bad work environment rather than unemployment.

The present study has several limitations. First, the external validity of the findings is not guaranteed given that they were obtained in a cohort of participants which was not representative of the French population. Second, occupational and social data as well as health status were self-reported and may therefore have been imprecise, despite the fact that the information on health status was collected by a physician. Third, as a consequence of self-

reporting, information on the occurrence of fatal cardiovascular events and cancers was not available and the diagnosis of these pathologies was relatively simple with no distinction for example between ischemic and hemorrhagic strokes or between the different types of skin cancers. Fourth, social position and work environment were assessed at the time of the inclusion and may have not reflected the conditions in which participants lived during most of their lifetime, even though a complete disconnection is unlikely. Finally, due to the retrospective design of the analyses, reverse causation cannot be ruled out but it is difficult to imagine how early occurrence of cardiovascular events and cancers could have strongly modified social position and created bad work environment for people benefiting from the protective French social security system. Likewise, reverse causation is unlikely for unemployment exposure given that the episodes occurred in average prior to the occurrence of cardiovascular events and cancers (supplemental Figure 3).

In conclusion, this study indicates that although low social position, bad work environment and unemployment exposure are tightly interrelated, they are associated with distinct cardiovascular and cancerous outcomes that could add up during lifetime and should therefore be considered all together to optimally design preventive strategies.

Author contributions: MSR performed statistical analyses, data interpretation and critical revision of the manuscript for important intellectual content; MP, GA and NH were involved in study concept and design and performed critical revision of the manuscript for important intellectual content; CR, MG and MZ obtained cohort funding and performed critical revision of the manuscript for important intellectual content; PM supervised the study and wrote the first draft of the manuscript. PM confirms that he had full access to all the data and has final responsibility for the decision to submit for publication.

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011). Participants gave informed written consent to participate in the study.

Data availability statement: Personal health data underlying the findings of our study are not publicly available due to legal reasons related to data privacy protection. However, the data are available upon reasonable request after approval from the French National Data Protection Authority. The email address for any inquiry is contact@constances.fr.

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Figure 1: Multiple correspondence analysis showing the association between social position, work environment and unemployment duration. The plot uses the two first dimensions which explain respectively 23.4 and 17.6% of the total inertia (81.7 and 21.6% with Greenacre adjustment).

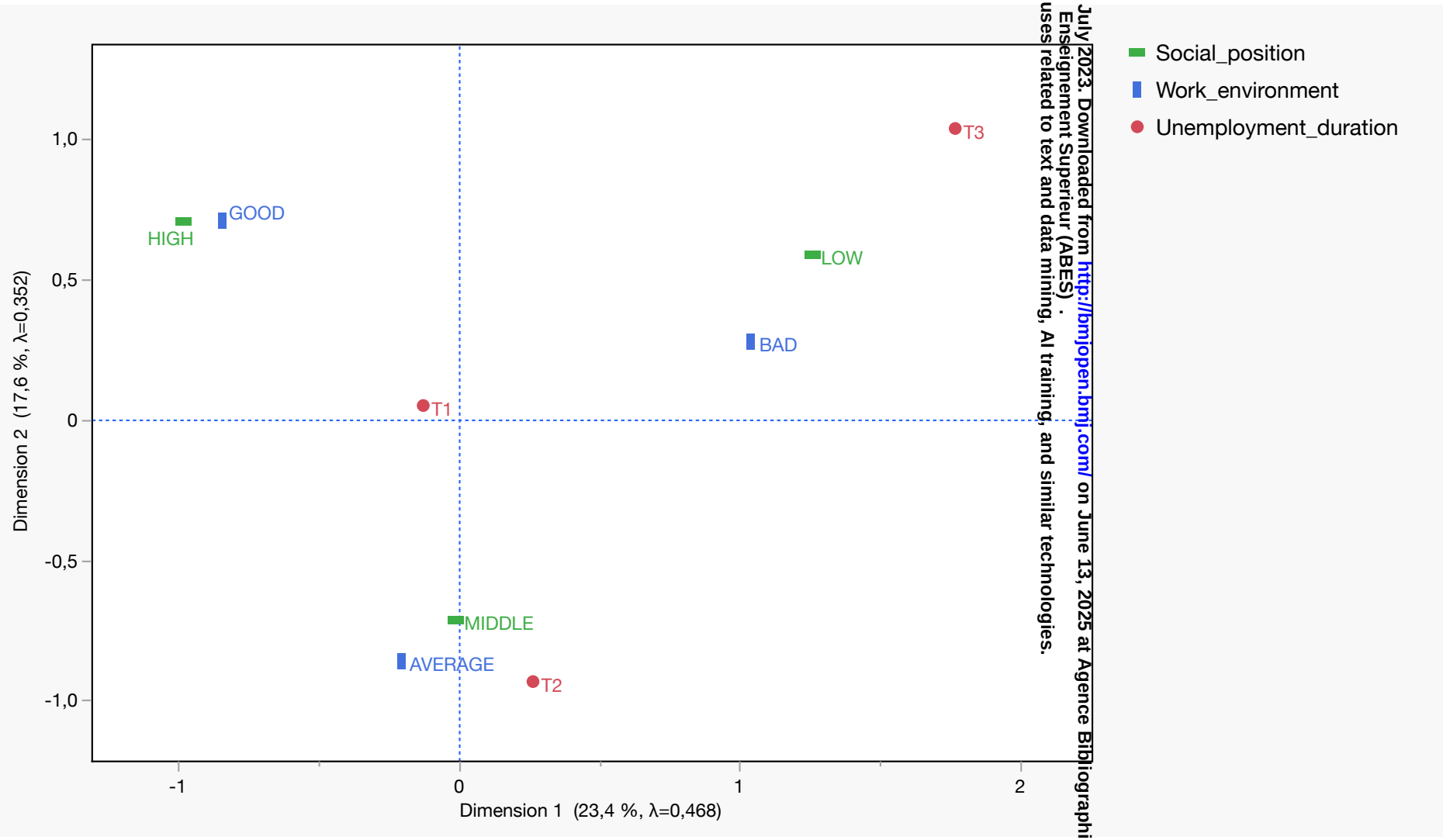


Table S1: Characteristics of cohort participants with or without missing values compared to randomly selected individuals from the French population.

		Representative sample of the French population		Whole cohort		Cohort without missing value		Comparing representative sample of the French population and whole cohort	Comparing representative sample of the French population and cohort without missing value	Comparing whole cohort and cohort without missing value
		n	%	n	%	n	%	Cohen's h	Cohen's h	Cohen's h
-	**All**	24,242	-	205,203	-	130,197	-	-	-	-
Sex	**Women**	12,745	52.6	110,193	53.7	66,743	51.3	-0.022	0.026	0.048
	Men	11,497	47.4	95,010	46.3	63,454	48.7	0.022	-0.026	-0.048
Age (y)	**18-39**	9657	39.9	66,832	32.6	46,892	36.0	0.152	0.080	-0.072
	40-54	7717	31.8	69,100	33.6	43,443	33.4	-0.038	-0.034	0.004
	55-75	6868	28.4	69,271	33.8	39,862	30.6	-0.117	-0.048	0.069
Education	**University**	6022	24.9	118,646	58.9	82,930	64.2	-0.705**	0.814***	-0.109
	Secondary school	11,643	48.0	33,246	16.5	20,748	16.1	0.694**	0.705**	0.011
	Primary school	6577	27.1	49,538	24.6	25,431	19.7	0.057	0.175	0.118
Occupation	**Management**	3103	15.5	58,441	32.2	42,099	35.8	-0.398*	-0.474*	-0.076
	Intermediate	5060	25.2	54,114	29.9	35,885	30.6	-0.105	-0.121	-0.015
	Blue collar/clerk	11,900	59.3	68,817	37.9	39,505	33.6	0.432*	0.521**	0.090

The percentages were calculated relatively to the number of cohort participants with or without missing values or of individuals randomly selected from the French population; Each pair of proportions was compared using Cohen's h, measure of effect size with the rule of thumb to categorize substantial differences as *small ($0.2 \leq h < 0.5$), **medium ($0.5 \leq h > 0.8$) ; ***large ($h \geq 0.8$).

Table S2: Indicators of social position of participants at inclusion.

		n	%
Education (y)	**≥17**	35,557	27.5
	14-16	47,373	36.7
	12-13	20,748	16.1
	≤11	25,431	19.7
Occupation	**Management**	42,099	35.8
	Intermediate	35,885	30.6
	Blue collar/clerk	39,505	33.6
Income	**Very high**	39,952	32.6
	High	40,396	32.9
	Middle	31,339	25.5
	Low	11,019	9.0
Spouse occupation	**Management**	32,048	34.7
	Intermediate	25,037	27.1
	Blue collar/clerk	35,268	38.2
Social vulnerability	**Low**	40,116	30.9
	Average	45,849	35.4
	High	43,729	33.7

The percentages were calculated relatively to the total number of participants in the cohort.

Figure S1: Multiple correspondence analysis showing the association between the different indicators used to characterize social position of participants at inclusion. The plot uses the two first dimensions which explain respectively 18.3 and 11.7% of the total inertia (6.0 and 8.9% with Greenacre adjustment).

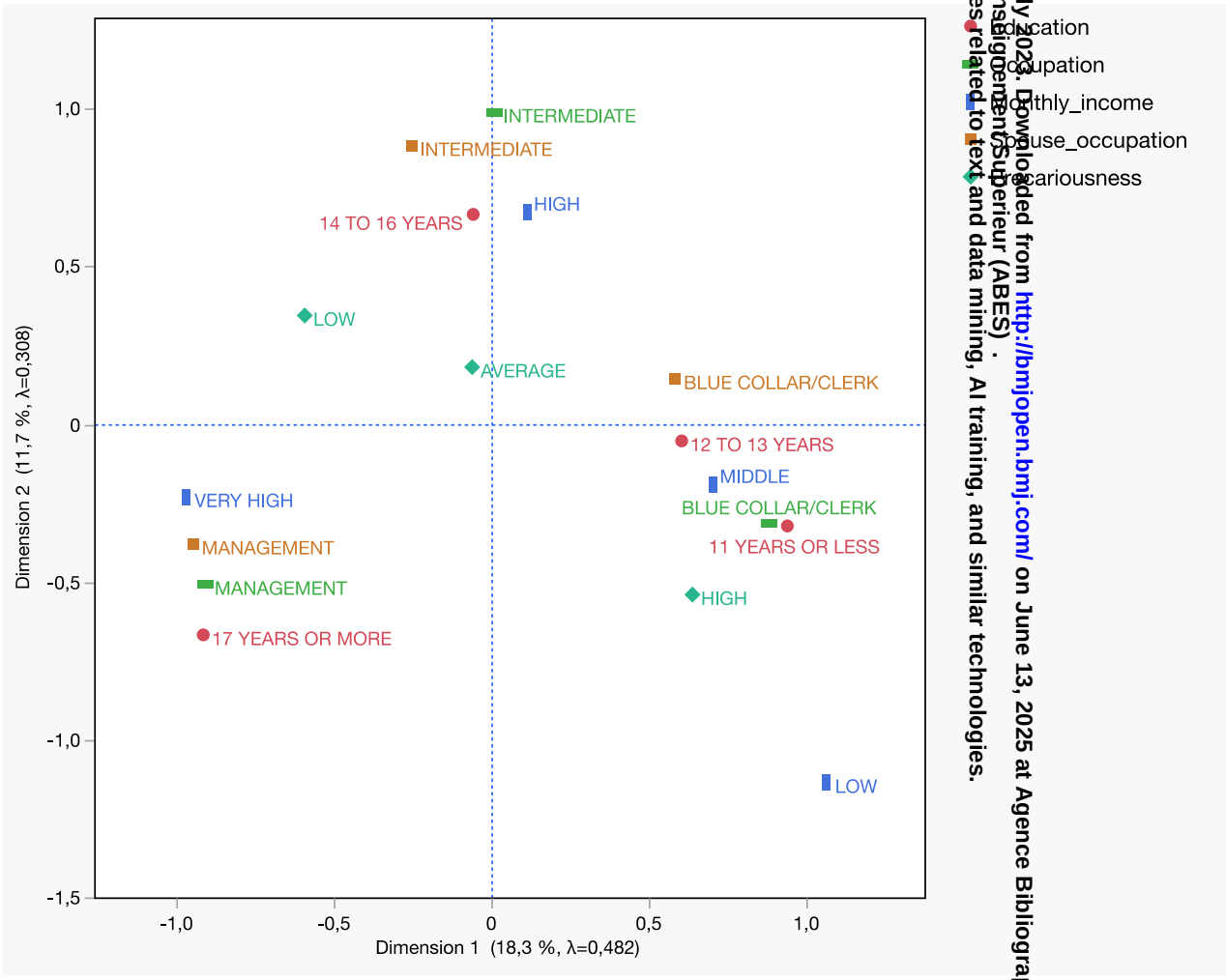


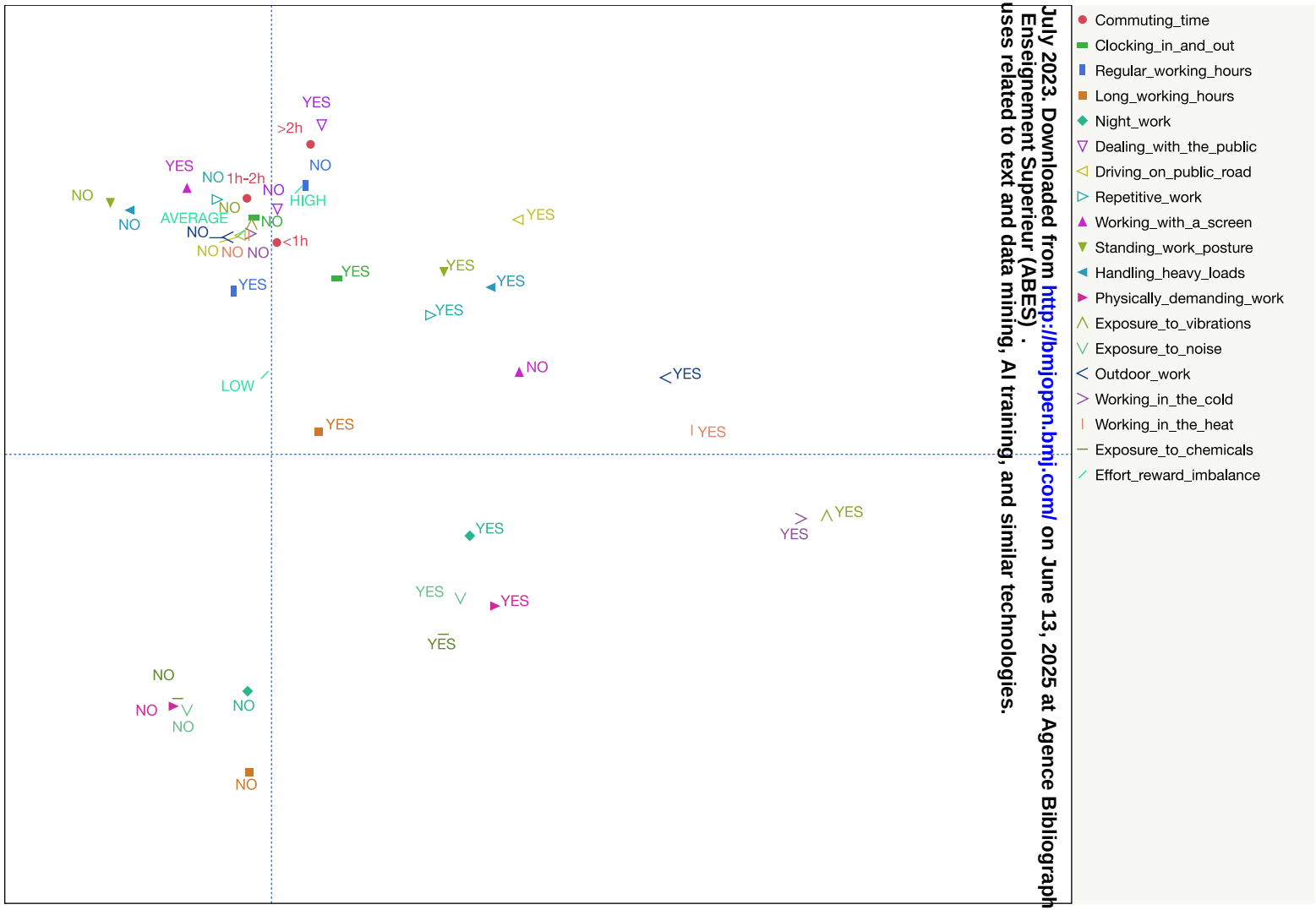
Table S3: Indicators of work environment of participants at inclusion.

		n	%
Commuting time	<1h	72,604	76.4
	1h-2h	18,757	19.7
	>2h	3648	3.9
Clocking in and out	No	74,281	77.8
	Yes	21,186	22.2
Regular working hours	No	53,085	55.4
	Yes	42,755	44.6
Long working hours	No	91,576	70.3
	Yes	38,621	29.7
Night work	No	118,011	90.6
	Yes	12,186	9.4
Dealing with the public	No	47,177	71.5
	Yes	18,801	28.5
Driving on public road	No	84,666	88.1
	Yes	11,397	11.9
Repetitive work	No	71,866	76.2
	Yes	22,401	23.8
Working with a screen	No	22,353	23.4
	Yes	73,266	76.6
Standing work posture	No	50,917	52.9
	Yes	45,246	47.1
Handling heavy loads	No	59,662	62.3
	Yes	36,112	37.7
Physically demanding work	No	93,933	72.2
	Yes	36,264	27.8
Exposure to vibrations	No	91,992	96.6
	Yes	3290	3.4
Exposure to noise	No	92,000	70.7
	Yes	38,197	29.3
Outdoor work	No	87,810	90.2

	Yes	9492	9.8
Working in the cold	No	93,155	96.8
	Yes	3075	3.2
Working in the heat	No	92,140	95.6
	Yes	4257	4.4
Exposure to chemicals	No	86,472	66.4
	Yes	43,725	33.6
Effort-reward imbalance	Low	30,381	31.8
	Average	36,199	37.9
	High	28,940	30.3

The percentages were calculated relatively to the total number of participants in the cohort.

Figure S2: Multiple correspondence analysis showing the association between the different occupational exposures used to characterize work environment of participants at inclusion. The plot uses the two first dimensions which explain



respectively 16.8 and 12.0% of the total inertia (43.5 and 17.8% with Greenacre adjustment)

Table S4: Adjusted odds ratios (95% confidence interval, p) for the prevalence of cardiovascular events or cancers in participants at inclusion according to their exposure to common risk factors.

		Cardiovascular event		Cancer	
Sex	Women	1.00		1.00	
	Men	2.32 (2.09-2.58)	<0.0001	0.61 (0.58-0.65)	<0.0001
Age (y)	18-39	1.00		1.00	
	40-54	3.17 (2.50-4.02)	<0.0001	3.30 (2.94-3.70)	<0.0001
	55-75	6.72 (5.34-8.46)	<0.0001	8.60 (7.70-9.61)	<0.0001
Parental history of cardiovascular event	No	1.00		1.00	
	Yes	1.31 (1.20-1.44)	<0.0001	0.97 (0.92-1.03)	0.39
Parental history of cancer	No	1.00		1.00	
	Yes	0.94 (0.86-1.03)	0.21	1.28 (1.22-1.35)	<0.0001
Lifetime non-moderate alcohol consumption	Rarely	1.00		1.00	
	Sometimes	0.95 (0.80-1.12)	0.51	0.99 (0.91-1.09)	0.95
	Often	0.90 (0.78-1.03)	0.12	0.94 (0.87-1.02)	0.12
Smoking	Never	1.00		1.00	
	Former	1.48 (1.34-1.63)	<0.0001	1.10 (1.04-1.17)	0.001
	Current	1.37 (1.19-1.57)	<0.0001	0.85 (0.78-0.92)	0.0002
Leisure-time physical inactivity	No	1.00		1.00	
	Yes	1.09 (0.94-1.27)	0.24	1.00 (0.91-1.11)	0.93
Body mass index	Optimal	1.00		1.00	
	Overweight	1.05 (0.94-1.16)	0.39	0.95 (0.89-1.01)	0.09
	Obesity	0.99 (0.87-1.12)	0.83	0.93 (0.85-1.01)	0.09
Hypertension	No	1.00		1.00	
	Yes	2.17 (1.96-2.39)	<0.0001	1.05 (0.97-1.24)	0.19
Dyslipidemia	No	1.00		1.00	
	Yes	5.89 (5.34-6.49)	<0.0001	1.07 (0.98-1.37)	0.11
Diabetes	No	1.00		1.00	
	Yes	1.11 (0.94-1.31)	0.20	1.11 (0.94-1.30)	0.22
Sleep disorders	No	1.00		1.00	
	Yes	1.15 (1.05-1.26)	0.003	1.16 (1.09-1.23)	<0.0001
Depression	No	1.00		1.00	
	Yes	1.29 (1.14-1.46)	<0.0001	1.09 (1.01-1.18)	0.03

Models were adjusted for sex, age, parental history of cardiovascular event, parental history of cancer, social position, work environment, unemployment duration, lifetime non-moderate

alcohol consumption, smoking, leisure-time physical inactivity, body mass index, hypertension, dyslipidemia, diabetes, sleep disorders and depression.

Table S5: Adjusted odds ratios (95% confidence interval) for the prevalence of specific non-fatal cancers in participants at inclusion according to unemployment duration.

Body location	Unemployment duration (quarters)	n	%	Models 1	p	Models 2	p	Models 3	p
All	0	5018	4.50	1.00		1.00		1.00	
	1-19	532	4.19	0.95 (0.86-1.04)	0.25	0.95 (0.87-1.04)	0.37	0.95 (0.87-1.05)	0.31
	20-148	380	6.24	0.98 (0.88-1.09)	0.71	0.96 (0.86-1.07)	0.47	0.96 (0.86-1.07)	0.44
Breast	0	1300	1.17	1.00		1.00		1.00	
	1-19	162	1.28	1.02 (0.86-1.21)	0.80	1.04 (0.88-1.23)	0.66	1.03 (0.87-1.22)	0.73
	20-148	128	2.10	1.03 (0.85-1.24)	0.79	1.02 (0.84-1.23)	0.86	1.01 (0.83-1.22)	0.94
Skin	0	1267	1.14	1.00		1.00		1.00	
	1-19	129	1.02	0.92 (0.76-1.10)	0.35	0.95 (0.79-1.15)	0.62	0.96 (0.80-1.15)	0.67
	20-148	69	1.13	0.72 (0.56-0.92)	0.009	0.77 (0.60-0.98)	0.03	0.78 (0.61-1.01)	0.06
Prostate	0	611	0.55	1.00		1.00		1.00	
	1-19	39	0.31	0.72 (0.52-1.00)	0.05	0.75 (0.54-1.04)	0.09	0.76 (0.55-1.06)	0.11
	20-148	34	0.56	0.92 (0.65-1.31)	0.65	0.91 (0.64-1.29)	0.59	0.94 (0.66-1.33)	0.71
Cervical	0	254	0.23	1.00		1.00		1.00	
	1-19	38	0.30	1.19 (0.85-1.68)	0.31	1.15 (0.81-1.61)	0.44	1.11 (0.78-1.56)	0.56
	20-148	33	0.54	1.54 (1.07-2.22)	0.02	1.36 (0.94-1.97)	0.10	1.26 (0.87-1.83)	0.22
Colon	0	259	0.23	1.00		1.00		1.00	
	1-19	33	0.26	1.22 (0.85-1.76)	0.28	1.24 (0.86-1.79)	0.24	1.23 (0.85-1.78)	0.26
	20-148	19	0.31	0.95 (0.60-1.52)	0.84	0.92 (0.57-1.47)	0.71	0.92 (0.57-1.47)	0.72
Thyroid	0	270	0.24	1.00		1.00		1.00	
	1-19	36	0.28	1.12 (0.79-1.59)	0.52	1.10 (0.78-1.56)	0.59	1.11 (0.78-1.57)	0.57
	20-148	19	0.31	0.89 (0.56-1.43)	0.64	0.84 (0.53-1.35)	0.48	0.87 (0.54-1.40)	0.56

Lymphoma	**0**	263	0.24	1.00		1.00		1.00	
	1-19	23	0.18	0.79 (0.52-1.22)	0.29	0.79 (0.52-1.21)	0.28	0.79 (0.51-1.21)	0.27
	20-148	18	0.30	1.11 (0.68-1.79)	0.67	1.08 (0.67-1.76)	0.75	1.07 (0.66-1.74)	0.78
Lung	**0**	69	0.06	1.00		1.00		1.00	
	1-19	4	0.03	0.56 (0.20-1.54)	0.26	0.53 (0.19-1.47)	0.22	0.50 (0.18-1.38)	0.18
	20-148	5	0.08	1.08 (0.43-2.68)	0.87	0.92 (0.37-2.30)	0.86	0.84 (0.33-2.11)	0.71

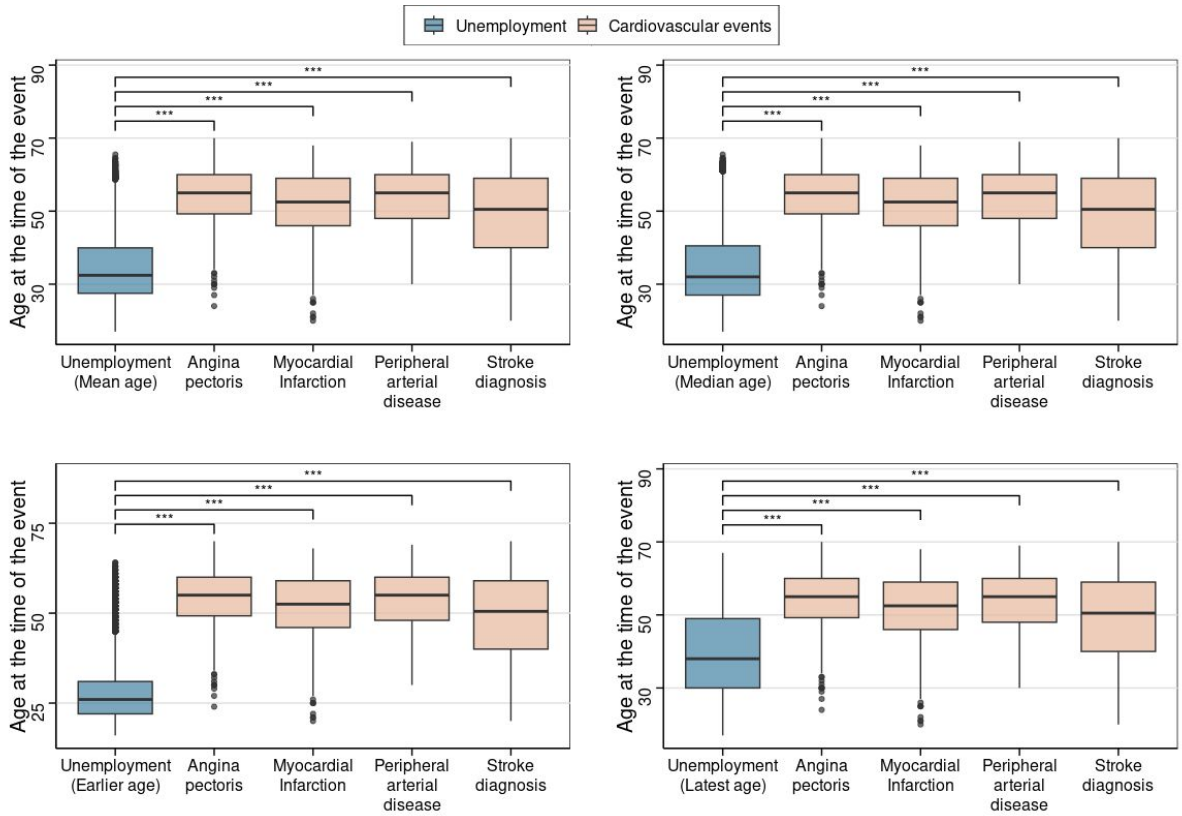
The percentages were calculated relatively to the number of participants for each unemployment duration (0 quarter=111,407; 1-19 quarters=12,702; 20-148 quarters=6088).

Models 1 were adjusted for sex, age and parental history of cancer.

Models 2 were adjusted for sex, age, parental history of cancer, social position and work environment.

Models 3 were adjusted for sex, age, parental history of cancer, work environment, unemployment duration, lifetime non-moderate alcohol consumption, smoking, body mass index and sleep disorders.

Figure S3: Age differences between the occurrence of unemployment episodes and cardiovascular events during the lifetime of participants. The age at which unemployment episodes occurred was expressed in four different ways: mean, median, earlier or latest age. In each box plot, the horizontal line represents the median value, the ends of the box represent the 1st and 3rd quartiles and the length of the box is the interquartile range, the lines on each end of the box extend to the outermost values that fall within 1st quartile -1.5*(interquartile range) and 3rd quartile + 1.5*(interquartile range), the values below or above these boundaries are shown as individual outliers. The differences were assessed with the non-parametric Wilcoxon-Mann-Whitney test. * p<0.05; ** p<0.01; *** p<0.001.



STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	
Objectives	3	State specific objectives, including any prespecified hypotheses	5	
Methods				
Study design	4	Present key elements of study design early in the paper		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	thru 11	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	thru 11	
Bias	9	Describe any efforts to address potential sources of bias	6 & 10	
Study size	10	Explain how the study size was arrived at	6	

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11 & 12
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11 & 12
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	6
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	13 & 14
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	15 thru 19
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15 thru 19
		(*b*) Report category boundaries when continuous variables were categorized	15 thru 19
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	20 & 21
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	21 & 22
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	20 & 21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	23

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Distinct cardiovascular and cancer burdens associated with social position, work environment and unemployment: a cross-sectional and retrospective study in a large population-based French cohort

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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Occupational and environmental medicine, Public health
Keywords:	EPIDEMIOLOGY, SOCIAL MEDICINE, OCCUPATIONAL & INDUSTRIAL MEDICINE, Cardiac Epidemiology < CARDIOLOGY, Epidemiology < ONCOLOGY

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Distinct cardiovascular and cancer burdens associated with social position, work environment and unemployment: a cross-sectional and retrospective study in a large population-based French cohort

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ABSTRACT

Objectives: Distinguish the respective effects of social position, work environment and unemployment on cardiovascular and cancer risks.

Design: A cross-sectional and retrospective observational study.

Setting: A population-based French cohort (CONSTANCES).

Participants: 130,197 adults enrolled between 2012 and 2021 without missing values.

Primary outcome measures: The associations of social position, work environment and unemployment exposure with the prevalence of cardiovascular events and cancers simultaneously tested using logistic regression models adjusting for common risk factors.

Results: While social position, work environment and unemployment exposure are strongly interrelated with each other, they are not linked to the same cardiovascular and cancer outcomes. Low social position and long unemployment duration are significantly associated with an increased prevalence of angina pectoris, myocardial infarction and peripheral arterial disease (OR=1.22 to 1.90, $p<0.04$ to <0.0001) but not of stroke. In contrast, bad work environment is associated with an increased prevalence of stroke (OR=1.29, $p<0.01$) but not of angina pectoris, myocardial infarction and peripheral arterial disease. Low social position is associated with an increased prevalence of cervical and lung cancers (OR=1.73 and 1.95,

p<0.002 and <0.03) and a decreased prevalence of skin cancer (OR=0.70, p<0.0001) while bad work environment is associated with an increased prevalence of breast, skin, prostate and colon cancers (OR=1.31 to 2.91, p<0.0002 to <0.0001). Unemployment exposure is not associated with the prevalence of any type of cancers.

Conclusions: Social position, work environment and unemployment are associated with distinct cardiovascular and cancerous diseases that could add up during lifetime, they should therefore be considered all together in any preventive strategy.

KEYWORDS

French cohort · retrospective study · social position · work environment · unemployment · cardiovascular event · cancer

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study analyzed recent data collected from a large population-based cohort.

- The respective effects of social position, work environment and unemployment on the prevalence of cardiovascular diseases and cancers were simultaneously tested with multiple logistic regression models adjusting for common confounders.

- Both social position and work environment were globally assessed using a wide array of indicators.

- As the cohort was not totally representative of the general population, the external validity of the findings is not warranted.

- The observational and retrospective nature of the study restricts the possibility of drawing causality.

INTRODUCTION

Social position is a powerful determinant of health, influencing the risk of cardiovascular diseases and cancers in particular.[1–4] The reasons why individuals with low social position usually have higher cardiovascular and cancer risks are many, including material deprivation, limited educational and cultural attainment, easy adoption of unhealthy behaviors, low importance given to the care of one's own health, inability to cope with illness and to access health care. For example, individuals with low social position, as measured by educational level, occupational class or income, are more likely to be exposed to several risk factors such as smoking, alcohol consumption, leisure-time physical inactivity, obesity, diabetes, hypertension, dyslipidemia, depression or sleep disorders.[5–13]

Work environment is another strong determinant of health.[14] Individuals with bad working conditions, as assessed by various physicochemical, biomechanical, organizational or psychosocial indicators, have higher cardiovascular and cancer risks.[15–17] Besides the health effects of bad working conditions, these individuals are also overexposed to common risk factors, including alcohol consumption, smoking, leisure-time physical inactivity, obesity, hypertension, diabetes, depression or sleep disorders.[8, 18–25]

Unemployment can also influence heath, independently from social position and work environment.[26–28] The reasons why unemployed individuals have higher cardiovascular and cancer risks[29–33] remain elusive but overexposure to risk factors, such as alcohol consumption, smoking, leisure-time physical inactivity, unbalanced diet, obesity, diabetes, depression or sleep disorders, is likely involved.[34–40]

Health burdens associated with low social position, bad work environment or unemployment are rarely assessed by taking into account these three conditions simultaneously, yet they are strongly interrelated[8, 41] and often exert their effects in a cumulative way during the lifetime of

individuals. The burden linked to one condition could be explained in part by the confounding of the other conditions. For example, the gradient in the incidence of behavioral risk factors (alcohol consumption, smoking, leisure-time physical inactivity) according to work environment is largely mediated by social position while the social gradient in the incidence of clinical risk factors (obesity, hypertension, dyslipidemia, diabetes, sleep disorders, depression) is rather mediated by work environment.[8]. Another potential issue is that social position and work environment are often characterized by a limited number of indicators, such as educational level, occupational class, income, job strain, night shift or chemical exposure, and are not considered as a whole, which is reality for individuals who are not facing only one or a few social constraints or occupational exposures.

The aim of this retrospective study was to simultaneously assess the relationships between the prevalence of cardiovascular events and cancers, unemployment exposure and global estimates of social position and work environment in a large population-based cohort. Examining whether these interrelated socioeconomic variables are associated to distinct health burdens that could add up during lifetime may be helpful to optimally design preventive strategies.

METHODS

Study population

205,203 adults who were affiliated to the general health insurance system (which covers 85% of the French population) were enrolled in the CONSTANCES cohort between February 2012 and September 2021 using a random sampling scheme stratified on age, sex, socioeconomic status and region.[42] Inclusion criteria comprised the obligation to provide written informed consent, to undergo a comprehensive health examination in one of the twenty-one participating medical centers scattered across metropolitan territory and to complete questionnaires on lifestyle, health-related behaviors, social and occupational conditions. The inclusion rate was rather low (7.3%)[43] in line with those observed in other large population-based cohorts when participants are required to visit a medical center for health-related exams.[44] Note that the authors of the present study did not have access to information that could have identified individual participants during or after data collection. Participants were not involved in the design of this study, nor in its implementation but they will be informed of the results. The cohort received approvals from the Ethics Evaluation Committee of the French National Institute of Health and Medical Research and from the National Committee for the Protection of Privacy and Civil Liberties.

The analyses were performed in a subset of 130,197 participants who had no missing values in all variables that were included in multi-adjusted regression models. The choice of selecting these participants rather than imputing randomly distributed missing data was driven by the fact that the cohort was not representative of the French population due to the low inclusion rate that resulted in the selection of socially privileged people, even though the stratified sampling strategy tried to compensate for the higher non-response rate of individuals with low socioeconomic status.[42] The selection of participants with no missing values only marginally accentuated this bias (supplemental Table 1) and the alternative of using multivariate imputation by chained equations would not have been devoid of other biases.[45]

Patient and public involvement

Participants or members of the public were not involved in the design of this study, nor in its implementation. Participants and general public will be informed of the results of the study through publication.

Social position of participants

Several socioeconomic indicators whose distributions are shown in supplemental Table 2 were considered for assessing social position of participants at inclusion. Educational attainment was classified into four levels depending on the number of years of study: ≤11, 12-13, 14-16 or ≥17. Occupation of participants and spouses was reduced from a ten-level classification in the original inquiry to three grades: blue collar/clerk, intermediate and management. Income that

included monthly earnings of all household members was ranked as low (below 1500 euros), middle (between 1500 and 2800 euros), high (between 2800 and 4200 euros) or very high (above 4200 euros). These thresholds were dictated by the inquiry that originally included seven levels of income and the need to balance the number of participants between groups. Social vulnerability was evaluated by a score that was calculated from a questionnaire comprising 11 binary items (Y/N) exploring material and social deprivation:[46] "do you sometimes meet a social worker?", "do you have complementary health insurance?", "do you live as a couple?", "are you a homeowner?", "are there periods in the month when you have real financial difficulties to meet your basic needs?", "have you done any sports activities in the last 12 months?", "have you been to any show over the last 12 months?", "have you been on holiday over the last 12 months?", "have you seen any family member over the last six months?", "if you have difficulties, is there anyone around who could take you in for a few days?", "if you have difficulties, is there anyone around who could provide you with material assistance?". This score was categorized into terciles (low, intermediate or high social vulnerability) for the analyses. Note that participants who were unemployed at inclusion reported the occupation, income and social vulnerability status they had just before the unemployment episode.

Given that these different indicators assess complementary and interdependent aspects of social position (supplemental Figure 1), a global score was calculated by giving for each indicator a value of 1 to the least privileged group, 2 or 3 to intermediary groups and 3 or 4 to the most privileged group, depending if the indicator encompassed 3 or 4 levels, by summing the values and by dividing the sum by the number of available indicators for each participant. This global score was categorized into terciles (low, middle or high social position) for the analyses, as previously reported.[8]

Work environment of participants

A total of 19 occupational exposures whose distributions are shown in supplemental Table 3 were used to characterize work environment of participants at inclusion. These included a series of organizational, physical, biomechanical, chemical and psychosocial factors such as commuting time, clocking in and out, regular working hours (on daily and weekly basis), long working hours (over 10h per week day), night work, dealing with the public, driving on public road, repetitive work (imposed by a machine, a procedure or someone), working with a screen, standing work posture, handling heavy loads (over one kilogram), physically demanding work, exposure to vibrations, exposure to noise, outdoor work, working in the cold, working in the heat, exposure to chemicals and the scale assessing effort-reward imbalance of work that was divided into terciles (low, average or high imbalance).[47] Note that participants who were unemployed at inclusion reported the work environment they had just before becoming unemployed.

Work environment was considered as a whole, which is reality for workers who are not facing only one or a few occupational exposures.[48] For that purpose, the exposures that were significantly interrelated with each other (supplemental Figure 2) were combined into a global score that was calculated by giving for each exposure a value of 1 to the least exposed group, 3 to the more exposed group, and 2 to intermediary groups whenever the exposure encompassed 3 levels, by summing the values and by dividing the sum by the number of available exposures for each worker. This global score was categorized into terciles (bad, average or good work environment) for the analyses, as already described.[49]

Unemployment experienced by participants

Unemployment exposure of participants during their lifetime was documented by a questionnaire in which they were asked to report each time they had stopped working for a

period of more than six months and why (unemployment, health issue, other reason). The existence of past episodes of unemployment was confirmed for each participant by administrative data from the French national pension system which also provided the total number of unemployed quarters. This number, that was used to estimate the duration of unemployment experienced by each participant, was arbitrarily categorized into three groups (0, 1-19, 20-148 quarters) for the analyses.

Prevalence of risk factors among participants

Several risk factors commonly found in the population were assessed in participants at inclusion. These included four nonmodifiable factors: sex, age that was divided into terciles (18-39, 40-54, 55-75 years old) and parental histories of cardiovascular event or cancer coded as binary variables (Y/N). Three behavioral factors: smoking coded into three categories (current, former, never), lifetime non-moderate alcohol consumption (more than two or three drinks on the same day in women or men, respectively)[50] classified as rarely (never or less than one time per month), sometimes (two or three times per month) or often (one time or more per week), leisure-time physical inactivity whose inquiry was based on a three item questionnaire asking about regular practice of walking or cycling, practicing a sport or gardening or housekeeping over the past 12 months; each item was noted 0 if the answer was no, 1 if the practice was regular but low (less than 15 minutes for sport, or 2 hours for the two other items, per week), 2 if the practice was regular and higher; the score calculated by summing the three items ranged from 0 (not active at all) to 6 (very active) and was used to characterize leisure-time physical inactivity (participants with a score <2). Six clinical risk factors were also retained: body mass index, hypertension, dyslipidemia (either hypercholesterolemia or

hypertriglyceridemia), diabetes, sleep disorders and depression. The inquiry into the presence and the age of onset of hypertension, dyslipidemia, diabetes and sleep disorders, which were coded as binary variables (Y/N), was performed by physicians in the medical centers. Body mass index (BMI) was calculated from measured weight and height and coded into three categories (optimal if BMI <25 kg/m^2, overweight if 25≤ BMI <30 kg/m^2, obesity if BMI ≥30 kg/m^2). Depression was assessed using the Centre of Epidemiologic Studies Depression scale and defined as a score ≥19 in both sexes.[51]

As the validity of self-reported information, even when collected by physicians, can be questioned, the coherence of the relationships between common risk factors and the prevalence of cardiovascular events and cancers was tested (supplemental Table 4). The fact that most of the expected associations were observed after multi-adjustment was a good indication that the collected information was reliable. Notably, the associations of the prevalence of cardiovascular events with sex, age, parental history of cardiovascular event, smoking, hypertension, dyslipidemia, sleep disorders, depression and the associations of the prevalence of cancers with sex, age, parental history of cancer, former smoking and sleep disorders. In any case, if a bias was present, it would likely have been under-reporting with rates varying from one disorder to another: 95.2% for diabetes, 80.4% for hypertension, 77.8% for peripheral arterial disease, 72.4% for myocardial infarction, 71.4% for angina pectoris, 54.5% for stroke.[52]

Prevalence of cardiovascular events and cancers among participants

During the visit in the medical centers at inclusion, physicians inquired about any non-fatal cardiovascular event and cancer that occurred during the lifetime of participants. Four types of cardiovascular events, coded as binary variables (Y/N), were retained for the analyses: stroke, angina pectoris, myocardial infarction and peripheral arterial disease. The information on the occurrence of any type of cancers was collected but only eight based on body location (breast,

skin, prostate, cervical, colon, thyroid, lymphoma, lung), coded as binary variables (Y/N), were analyzed separately due to the limited number of cases in the other locations.

Statistical analyses

The characteristics of participants with or without missing values or of individuals randomly selected from the French population were compared by pairs using Cohen's h measure of effect size with the rule of thumb to categorize substantial differences as small ($0.2 \leq h < 0.5$), medium ($0.5 \leq h > 0.8$) or large ($h \geq 0.8$).[53]

The characteristics of participants according to the past occurrence of cardiovascular event or cancer during their lifetime were compared by calculating standardized mean differences (SMD); values > 0.1 being considered as showing significant differences.[54]

The analyses were cross-sectional using the data collected at inclusion of participants but also retrospective because some data, such as cumulated unemployment duration or non-moderate alcohol consumption during lifetime, described past events. The associations between social position, work environment, unemployment duration and the prevalence of cardiovascular events and cancers were tested with multiple logistic regression modeling. Several types of models were used: models 1 were adjusted for sex, age and parental history of cardiovascular event or cancer; models 2 were adjusted for sex, age, parental history of cardiovascular event or cancer, social position, work environment and unemployment duration; models 3 were adjusted for sex, age, parental history of cardiovascular event, social position, work

environment, unemployment duration, lifetime non-moderate alcohol consumption, smoking, leisure-time physical inactivity, body mass index, hypertension, dyslipidemia, diabetes, sleep disorders and depression when investigating the prevalence of cardiovascular events, or for sex, age, parental history of cancer, social position, work environment, unemployment duration, lifetime non-moderate alcohol consumption, smoking, body mass index and sleep disorders when investigating the prevalence of cancers.

Residual analyses were performed to assess the fit of the data, assumptions were checked and the potential influence of outliers was examined for all associations.[55] Statistical significance was fixed a priori at two-sided p-value <0.05.

All analyses were performed with the statistical discovery software JMP 17 Pro (SAS, Cary NC) except the calculation of SMD which was done with R software 4.2.2 and "tableone" package 0.13.2.[56]

RESULTS

Interrelationships between low social position, bad work environment and unemployment duration among participants

As shown in Figure 1, social position, work environment and unemployment duration during lifetime were highly correlated, the lower the social position, the worse the work environment and the longest the unemployment duration.

Characteristics of participants according to the occurrence of non-fatal cardiovascular events during lifetime

Compared to participants who never suffered from cardiovascular event, those who did (2340 participants representing 1.8% of the cohort) were more likely to be old men with parental history of cardiovascular event, low social position, bad work environment and long exposure to unemployment (Table 1). They were also overexposed to several risk factors, including lifetime non-moderate alcohol consumption, former smoking, high body mass index, hypertension, dyslipidemia and diabetes.

Table 1: Characteristics of participants who have or have not had a cardiovascular event.

		Cardiovascular event				SMD
		No		Yes		
		n	%	n	%	
-	**All**	127,857	98.2	2340	1.8	-
Sex	**Women**	66,147	51.7	596	25.5	0.560
	Men	61,710	48.3	1744	74.5	
Age (y)	**18-39**	42,048	32.9	87	3.7	1.147
	40-54	43,890	34.3	380	16.3	
	55-75	41,919	32.8	1873	80.0	
Parental history of cardiovascular event	**No**	97,502	76.3	1334	57.0	0.417
	Yes	30,355	23.7	1006	43.0	
Social position	**High**	37,520	29.3	419	17.9	0.384
	Middle	61,212	47.9	1015	43.4	
	Low	29,125	22.8	906	38.7	
Work environment	**Good**	40,354	31.6	386	16.5	0.662
	Average	46,701	36.5	473	20.2	
	Bad	40,802	31.9	1481	63.3	
Unemployment duration (quarters)	**0**	109,461	85.6	1946	83.2	0.162
	1-19	12,507	9.8	195	8.3	
	20-148	5889	4.6	199	8.5	
Lifetime non-moderate alcohol consumption	**Rarely**	18,104	14.2	272	11.6	0.165
	Sometimes	26,826	21.0	373	15.9	
	Often	82,927	64.8	1695	72.5	
Smoking	**Never**	59,425	46.5	704	30.1	0.432
	Former	43,778	34.2	1287	55.0	
	Current	24,654	19.3	349	14.9	
Leisure-time physical inactivity	**No**	116,132	90.8	2120	90.6	0.008
	Yes	11,725	9.2	220	9.4	
Body mass index	**Optimal**	75,836	59.3	793	33.9	0.539
	Overweight	38,037	29.8	1021	43.6	
	Obese	13,984	10.9	526	22.5	
Hypertension	**No**	116,148	90.8	1295	55.3	0.874
	Yes	11,709	9.2	1045	44.7	
Dyslipidemia	**No**	119,939	93.8	1095	46.8	1.200
	Yes	7918	6.2	1245	53.2	
Diabetes	**No**	126,156	98.7	2113	90.3	0.373
	Yes	1701	1.3	227	9.7	
Sleep disorders	**No**	46,997	36.8	784	33.5	0.068
	Yes	80,860	63.2	1556	66.5	
Depression	**No**	109,684	85.8	1967	84.1	0.048
	Yes	18,173	14.2	373	15.9	

The percentages were calculated relatively to the number of participants who have or have not had a cardiovascular event; the differences between the two groups were assessed by computing standardized mean differences (SMD).

Prevalence of non-fatal cardiovascular events among participants according to social position, work environment and unemployment duration

Low social position was associated with an increased prevalence of cardiovascular events (OR from 1.22 to 1.90) except stroke whose association was non-significant after adjustment for risk factors, work environment and unemployment duration (Table 2).

Bad work environment was only associated with an increased prevalence of stroke (OR=1.29) (Table 2). Associations with angina pectoris, myocardial infraction and peripheral arterial disease were non-significant after adjustment for risk factors, social position and unemployment duration.

After adjustment for risk factors, social position and work environment, long duration of unemployment (20 to 148 quarters) was associated with an increased prevalence of cardiovascular events (OR from 1.46 to 1.70) except stroke whose association was non-significant whatever the adjustment (Table 2).

Table 2: Adjusted odds ratios (95% confidence interval) for the prevalence of non-fatal cardiovascular events in participants at inclusion according to their social position, work environment and unemployment exposure.

		Type of event	n	%	Models 1	p	Models 2	p	Models 3	p
Social position	High	All	419	1.10	1.00		1.00		1.00	
	Middle		1015	1.63	1.41 (1.25-1.58)	<0.0001	1.26 (1.12-1.42)	0.0001	1.13 (1.00-1.27)	0.05
	Low		906	3.02	2.01 (1.78-2.26)	<0.0001	1.63 (1.44-1.86)	<0.0001	1.27 (1.12-1.45)	0.0003
	High	Stroke	195	0.51	1.00		1.00		1.00	
	Middle		395	0.63	1.18 (0.99-1.40)	0.06	1.08 (0.91-1.29)	0.37	1.01 (0.84-1.20)	0.95
	Low		308	1.03	1.57 (1.31-1.89)	<0.0001	1.35 (1.11-1.64)	0.003	1.09 (0.89-1.33)	0.38
	High	Angina pectoris	116	0.31	1.00		1.00		1.00	
	Middle		319	0.51	1.58 (1.27-1.96)	<0.0001	1.43 (1.15-1.78)	0.001	1.27 (1.02-1.59)	0.03
	Low		285	0.95	2.16 (1.74-2.69)	<0.0001	1.78 (1.41-2.25)	<0.0001	1.40 (1.10-1.78)	0.005
	High	Myocardial infarction	143	0.38	1.00		1.00		1.00	
	Middle		352	0.57	1.43 (1.18-1.75)	0.0003	1.28 (1.05-1.57)	0.01	1.11 (0.90-1.36)	0.34
	Low		326	1.09	2.04 (1.67-2.50)	<0.0001	1.65 (1.34-2.05)	<0.0001	1.22 (1.01-1.52)	0.04
	High	Peripheral arterial disease	34	0.09	1.00		1.00		1.00	
	Middle		97	0.16	1.64 (1.11-2.43)	0.01	1.46 (0.98-2.17)	0.06	1.23 (0.82-1.84)	0.31
	Low		128	0.43	3.40 (2.32-4.98)	<0.0001	2.69 (1.79-4.02)	<0.0001	1.90 (1.26-2.86)	0.002
Work environment	Good	All	386	0.95	1.00		1.00		1.00	
	Average		473	1.00	1.03 (0.90-1.18)	0.70	0.95 (0.83-1.09)	0.50	0.93 (0.80-1.07)	0.28
	Bad		1481	3.50	1.88 (1.67-2.11)	<0.0001	1.61 (1.42-1.82)	<0.0001	1.26 (1.10-1.43)	0.0005
	Good	Stroke	182	0.45	1.00		1.00		1.00	
	Average		218	0.46	1.04 (0.86-1.27)	0.66	1.01 (0.83-1.24)	0.90	0.99 (0.81-1.21)	0.93
	Bad		498	1.18	1.68 (1.40-2.01)	<0.0001	1.54 (1.28-1.86)	<0.0001	1.29 (1.06-1.56)	0.01
	Good	Angina pectoris	115	0.28	1.00		1.00		1.00	
	Average		126	0.27	0.90 (0.70-1.16)	0.41	0.81 (0.63-1.05)	0.12	0.80 (0.62-1.04)	0.09
	Bad		479	1.13	1.79 (1.45-2.21)	<0.0001	1.49 (1.19-1.86)	0.0004	1.09 (0.87-1.37)	0.46
	Good	Myocardial infarction	126	0.31	1.00		1.00		1.00	
	Average		164	0.35	1.05 (0.83-1.33)	0.65	0.96 (0.76-1.22)	0.76	0.93 (0.73-1.18)	0.54
	Bad		531	1.26	1.83 (1.49-2.23)	<0.0001	1.54 (1.24-1.90)	<0.0001	1.13 (0.91-1.40)	0.28
	Good	Peripheral arterial disease	38	0.09	1.00		1.00		1.00	
	Average		48	0.10	1.05 (0.69-1.61)	0.81	0.90 (0.58-1.38)	0.62	0.90 (0.58-1.38)	0.62
	Bad		173	0.41	2.16 (1.50-3.10)	<0.0001	1.55 (1.06-2.27)	0.02	1.21 (0.83-1.78)	0.32
Unemployment duration (quarters)	0	All	1946	1.75	1.00		1.00		1.00	
	1-19		195	1.54	1.00 (0.86-1.16)	0.97	0.98 (0.84-1.14)	0.78	0.96 (0.82-1.12)	0.62
	20-148		199	3.27	1.56 (1.34-1.82)	<0.0001	1.40 (1.21-1.64)	<0.0001	1.39 (1.18-1.63)	<0.0001
	0	Stroke	767	0.69	1.00		1.00		1.00	
	1-19		68	0.54	0.82 (0.64-1.06)	0.13	0.81 (0.63-1.04)	0.10	0.80 (0.63-1.04)	0.09
	20-148		63	1.03	1.18 (0.91-1.53)	0.22	1.08 (0.83-1.40)	0.58	1.08 (0.82-1.40)	0.59
	0	Angina pectoris	598	0.54	1.00		1.00		1.00	
	1-19		60	0.47	1.04 (0.80-1.36)	0.77	1.01 (0.78-1.33)	0.91	1.00 (0.76-1.32)	0.98
	20-148		62	1.02	1.61 (1.23-2.10)	0.0004	1.45 (1.11-1.90)	0.006	1.46 (1.11-1.92)	0.007
	0	Myocardial infarction	667	0.60	1.00		1.00		1.00	
	1-19		76	0.60	1.19 (0.94-1.52)	0.15	1.16 (0.91-1.48)	0.23	1.12 (0.88-1.44)	0.35
	20-148		78	1.28	1.89 (1.48-2.40)	<0.0001	1.71 (1.34-2.17)	<0.0001	1.64 (1.28-2.11)	<0.0001
	0	Peripheral arterial disease	204	0.18	1.00		1.00		1.00	
	1-19		25	0.20	1.25 (0.82-1.89)	0.30	1.17 (0.77-1.78)	0.45	1.08 (0.71-1.65)	0.71
	20-148		30	0.49	2.30 (1.56-3.39)	<0.0001	1.91 (1.29-2.82)	0.001	1.70 (1.14-2.53)	0.009

The percentages were calculated relatively to the number of participants for each social position (high=37,939; middle=62,227; low=30,031), work environment (good=40,740; average=47,174; bad=42,283) or unemployment duration (0 quarter=111,407; 1-19 quarters=12,702; 20-148 quarters=6088).

Models 1 included either social position, work environment or unemployment duration and were adjusted for sex, age and parental history of cardiovascular event.

Models 2 included social position, work environment and unemployment duration and were adjusted for sex, age and parental history of cardiovascular event.

Models 3 included social position, work environment and unemployment duration and were adjusted for sex, age, parental history of cardiovascular event, lifetime non-moderate alcohol consumption, smoking, leisure-time physical inactivity, body mass index, hypertension, dyslipidemia, diabetes, sleep disorders and depression.

Characteristics of participants according to the occurrence of non-fatal cancers during lifetime

Compared to participants who never suffered from cancer, those who did (5930 participants representing 4.6% of the cohort) were more likely to be old women with parental history of cancer, low social position and bad work environment (Table 3). They were also overexposed to risk factors such as former smoking, high body mass index and marginally sleep disorders.

Table 3: Characteristics of participants who have or have not had a cancer.

		Cancer				SMD
		No		Yes		
		n	%	n	%	
-	**All**	124,267	95.4	5930	4.6	-
Sex	**Women**	63,160	50.8	3583	60.4	0.118
	Men	61,107	49.2	2347	39.6	
Age (y)	**18-39**	41,738	33.6	397	6.7	0.920
	40-54	42,905	34.5	1365	23.0	
	55-75	39,624	31.9	4168	70.3	
Parental history of cancer	**No**	82,462	66.4	3088	52.1	0.282
	Yes	41,805	33.6	2842	47.9	
Social position	**High**	36,471	29.4	1468	24.7	0.151
	Middle	59,466	47.8	2761	46.6	
	Low	28,330	22.8	1701	28.7	
Work environment	**Good**	39,356	31.7	1384	23.3	0.441
	Average	45,771	36.8	1403	23.7	
	Bad	39,140	31.5	3143	53.0	
Unemployment duration (quarters)	**0**	106,389	85.6	5018	84.6	0.088
	1-19	12,170	9.8	532	9.0	
	20-148	5708	4,6	380	6.4	
Lifetime non-moderate alcohol consumption	**Rarely**	17,503	14.1	873	14.7	0.042
	Sometimes	25,994	20.9	1205	20.3	
	Often	80,770	65.0	3852	65.0	
Smoking	**Never**	57,498	46.3	2631	44.4	0.240
	Former	42,482	34.2	2583	43.6	
	Current	24,287	19.5	716	12.0	
Body mass index	**Optimal**	73,501	59.1	3128	52.8	0.165
	Overweight	37,093	29.9	1965	33.1	
	Obese	13,673	11.0	837	14.1	
Sleep disorders	**No**	45,861	36.9	1920	32.4	0.073
	Yes	78,406	63.1	4010	67.6	

The percentages were calculated relatively to the number of participants who have or have not had a cancer; the differences between the two groups were assessed by computing standardized mean differences (SMD).

Prevalence of non-fatal cancers among participants according to social position, work environment and unemployment duration

After adjustment for risk factors, work environment and unemployment duration, low social position was not associated with the prevalence of cancers when they were considered globally (Table 4). However, it was directly associated with cervical and lung cancers (OR=1.73 and 1.95 respectively) while it was strongly and inversely associated with skin cancer (OR=0.70).

After adjustment for risk factors, social position and unemployment duration, bad work environment was associated with an increased prevalence of cancers when they were considered globally (OR=1.45) (Table 4). More precisely, it was directly associated with breast, skin, prostate and colon cancers (OR from 1.31 to 2.91).

Unemployment duration was not associated with the prevalence of any type of cancers whatever the adjustment (supplemental Table 5).

Table 4: Adjusted odds ratios (95% confidence interval) for the prevalence of non-fatal cancers in participants at inclusion according to their social position and work environment.

		Body location	n	%	Models 1	p	Models 2	p	Models 3	p
Social position	High	All	1468	3.87	1.00		1.00		1.00	
	Middle		2761	4.44	1.05 (0.98-1.12)	0.16	0.97 (0.91-1.04)	0.47	0.97 (0.91-1.04)	0.44
	Low		1701	5.66	1.12 (1.04-1.21)	0.003	0.98 (0.91-1.06)	0.63	0.98 (0.91-1.07)	0.71
	High	Breast	385	1.01	1.00		1.00		1.00	
	Middle		753	1.21	1.00 (0.88-1.13)	0.99	0.95 (0.84-1.08)	0.44	0.95 (0.83-1.08)	0.42
	Low		452	1.51	1.08 (0.94-1.24)	0.29	0.99 (0.85-1.15)	0.87	0.99 (0.85-1.15)	0.88
	High	Skin	453	1.19	1.00		1.00		1.00	
	Middle		679	1.09	0.85 (0.75-0.96)	0.008	0.81 (0.71-0.92)	0.0008	0.83 (0.73-0.94)	0.003
	Low		333	1.11	0.71 (0.62-0.82)	<0.0001	0.65 (0.56-0.76)	<0.0001	0.70 (0.60-0.81)	<0.0001
	High	Prostate	146	0.38	1.00		1.00		1.00	
	Middle		306	0.49	1.18 (0.96-1.44)	0.11	0.91 (0.74-1.12)	0.38	0.92 (0.75-1.13)	0.44
	Low		232	0.77	1.23 (0.99-1.51)	0.06	0.82 (0.66-1.03)	0.09	0.84 (0.67-1.05)	0.12
	High	Cervical	60	0.16	1.00		1.00		1.00	
	Middle		162	0.26	1.53 (1.13-2.06)	0.005	1.48 (1.09-2.00)	0.01	1.41 (1.04-1.91)	0.03
	Low		103	0.34	2.01 (1.45-2.79)	<0.0001	1.86 (1.32-2.61)	0.0003	1.73 (1.22-2.44)	0.002
	High	Colon	61	0.16	1.00		1.00		1.00	
	Middle		146	0.23	1.29 (0.95-1.74)	0.10	1.12 (0.82-1.52)	0.47	1.12 (0.82-1.52)	0.48
	Low		104	0.35	1.43 (1.04-1.97)	0.03	1.14 (0.82-1.59)	0.44	1.15 (0.82-1.61)	0.42
	High	Thyroid	74	0.20	1.00		1.00		1.00	
	Middle		160	0.26	1.23 (0.93-1.62)	0.14	1.20 (0.91-1.60)	0.19	1.21 (0.91-1.61)	0.18
	Low		91	0.30	1.34 (0.98-1.84)	0.06	1.30 (0.94-1.80)	0.12	1.31 (0.94-1.83)	0.11
	High	Lymphoma	77	0.20	1.00		1.00		1.00	
	Middle		148	0.24	1.15 (0.87-1.51)	0.33	1.14 (0.86-1.52)	0.35	1.13 (0.85-1.50)	0.41
	Low		79	0.26	1.13 (0.82-1.56)	0.44	1.11 (0.79-1.56)	0.55	1.09 (0.77-1.54)	0.63
	High	Lung	13	0.03	1.00		1.00		1.00	
	Middle		32	0.05	1.40 (0.73-2.68)	0.30	1.35 (0.70-2.61)	0.37	1.24 (0.64-2.41)	0.52
	Low		33	0.11	2.36 (1.23-4.52)	0.01	2.23 (1.12-4.42)	0.02	1.95 (1.02-3.90)	0.03
Work environment	Good	All	1384	3.40	1.00		1.00		1.00	
	Average		1403	2.97	0.93 (0.86-1.01)	0.06	0.93 (0.86-1.01)	0.07	0.92 (0.85-1.01)	0.06
	Bad		3143	7.43	1.47 (1.37-1.57)	<0.0001	1.47 (1.37-1.58)	<0.0001	1.45 (1.35-1.56)	<0.0001
	Good	Breast	415	1.02	1.00		1.00		1.00	
	Average		377	0.80	0.93 (0.81-1.07)	0.34	0.93 (0.81-1.08)	0.34	0.92 (0.80-1.06)	0.26
	Bad		798	1.89	1.31 (1.16-1.49)	<0.0001	1.32 (1.16-1.50)	<0.0001	1.31 (1.15-1.49)	<0.0001
	Good	Skin	380	0.93	1.00		1.00		1.00	
	Average		362	0.77	0.86 (0.74-1.01)	0.06	0.90 (0.77-1.04)	0.14	0.91 (0.78-1.05)	0.19
	Bad		723	1.71	1.19 (1.04-1.35)	0.01	1.33 (1.16-1.53)	<0.0001	1.34 (1.16-1.54)	<0.0001
	Good	Prostate	68	0.17	1.00		1.00		1.00	
	Average		52	0.11	0.62 (0.43-1.01)	0.06	0.65 (0.45-1.01)	0.06	0.65 (0.45-1.02)	0.07
	Bad		564	1.33	2.72 (2.11-3.51)	<0.0001	2.90 (2.23-3.79)	<0.0001	2.91 (2.23-3.80)	<0.0001
	Good	Cervical	97	0.24	1.00		1.00		1.00	
	Average		95	0.20	0.97 (0.73-1.29)	0.86	0.93 (0.70-1.24)	0.63	0.92 (0.69-1.22)	0.56
	Bad		133	0.31	1.28 (0.97-1.70)	0.08	1.12 (0.84-1.50)	0.42	1.14 (0.86-1.52)	0.36
	Good	Colon	49	0.12	1.00		1.00		1.00	
	Average		58	0.12	1.08 (0.73-1.58)	0.70	1.06 (0.72-1.55)	0.77	1.05 (0.72-1.54)	0.80
	Bad		204	0.48	2.00 (1.45-2.76)	<0.0001	1.94 (1.39-2.70)	0.0001	1.90 (1.36-2.65)	0.0002
	Good	Thyroid	86	0.21	1.00		1.00		1.00	
	Average		103	0.22	1.14 (0.85-1.51)	0.38	1.11 (0.83-1.48)	0.47	1.09 (0.82-1.46)	0.54
	Bad		136	0.32	1.25 (0.94-1.66)	0.13	1.18 (0.88-1.59)	0.27	1.16 (0.86-1.56)	0.33
	Good	Lymphoma	90	0.22	1.00		1.00		1.00	
	Average		83	0.18	0.79 (0.59-1.07)	0.13	0.78 (0.58-1.06)	0.11	0.77 (0.57-1.04)	0.09
	Bad		131	0.31	1.07 (0.80-1.42)	0.64	1.03 (0.77-1.40)	0.83	1.01 (0.75-1.37)	0.92
	Good	Lung	14	0.03	1.00		1.00		1.00	
	Average		20	0.04	1.24 (0.62-2.46)	0.54	1.12 (0.56-2.24)	0.74	1.07 (0.54-2.15)	0.84
	Bad		44	0.10	1.62 (0.87-3.03)	0.13	1.29 (0.67-2.47)	0.45	1.24 (0.64-2.38)	0.52

The percentages were calculated relatively to the number of participants for each social position (high=37,939; middle=62,227; low=30,031) or work environment (good=40,740; average=47,174; bad=42,283).

Models 1 included either social position, work environment or unemployment duration and were adjusted for sex, age and parental history of cancer.

Models 2 included social position, work environment and unemployment duration and were adjusted for sex, age and parental history of cancer.

Models 3 included social position, work environment and unemployment duration and were adjusted for sex, age, parental history of cancer, lifetime non-moderate alcohol consumption, smoking, body mass index and sleep disorders.

Summary of the associations between social position, work environment, unemployment duration and the prevalence of non-fatal cardiovascular events and cancers

The significant associations after adjustment for risk factors and their putative directions are summarized in Figure 2.

Chronology of unemployment, non-fatal cardiovascular events and cancers during the lifetime of participants

In order to test the possibility of reverse causation where cardiovascular events or cancers would have preceded unemployment, the age of participants at which unemployed quarters were declared was compared with the age at which cardiovascular events and cancers occurred. It appears that unemployment episodes popped up much earlier than cardiovascular events or cancers with a mean difference of approximately 5 to 20. Thus, the mean age at which the episodes happened was 34.4 (SD 9.2) in comparison to the mean age of occurrence of stroke 49.2 (12.0), angina pectoris 53.8 (8.3), myocardial infarction 51.7 (9.0), peripheral arterial disease 53.7 (7.9), breast 49.0 (8.6), prostate 59.2 (4.9), cervical 38.1 (8.9), colon 52.8 (9.1), thyroid 41.4 (12.2) and lung 51.8 (11.1) cancers (Supplemental Figure 3).

Prevalence of non-fatal cardiovascular events and cancers among men and women according to social position, work environment and unemployment duration

The analyses by sex suggest that the associations are generally observed both in men and women (supplemental tables S6 and S7). It is difficult to know if the occasional lack of associations (angina pectoris with unemployment duration for example) or the differences in their magnitude (angina pectoris with social position for example) between the sexes were real or due to the significantly decreased statistical power. Note that the results concerning the

associations of non-fatal cancers with unemployment duration are not shown as none of them were statistically significant in both sexes.

DISCUSSION

The present analyses report the prevalence of cardiovascular events and cancers according to social position, work environment and unemployment exposure in a large population-based French cohort. The retrospective design of the study privileges a holistic approach in which a wide array of indicators is used to globally characterize social position and work environment in order to provide a better assessment of what people face in real life. The results show that social position, work environment and unemployment exposure are strongly interrelated with each other in a way where people are either all good or all bad. The public health issue therefore first arises from people who cumulate a low social position, a bad work environment and a long exposure to unemployment.

The main finding is that, despite their strong interrelationships, social position, work environment and unemployment exposure are not linked to the same cardiovascular and cancerous outcomes. Thus, low social position and long unemployment duration are associated with an increased prevalence of angina pectoris, myocardial infarction and peripheral arterial disease but not of stroke. In contrast, bad work environment is associated with an increased prevalence of stroke but not of angina pectoris, myocardial infarction and peripheral arterial disease. These results add to previously reported data[1, 2, 31] by clearly showing distinct effects of social position and unemployment on one side and work environment on the other side on the risk of cardiovascular events. They also echo the fact that social position and work environment do not predict the incidence of the same risk factors, i.e., mainly behavioral factors (non-moderate alcohol consumption, smoking, leisure-time physical inactivity) for social position, mostly clinical factors (obesity, hypertension, dyslipidemia, diabetes, sleep disorders, depression) for work environment.[8] Overall, these results point out the existence of distinct etiologic mechanisms underlying coronary/peripheral and cerebrovascular diseases with

potentially different risk factors.[57] From a public health viewpoint, considering social position, work environment and unemployment exposure as risk factors remains of little practical interest to prevent cardiovascular events as they are hardly modifiable. However, they can indicate the need for more thorough monitoring of risk factors in people who cumulate low social position, bad work environment and long exposure to unemployment.

A similar conclusion can be drawn from the results showing that social position and work environment are not associated with the same types of cancers. While low social position is associated with an increased prevalence of cervical and lung cancers and a decreased prevalence of skin cancer, bad work environment is associated with an increased prevalence of breast, skin, prostate and colon cancers. These findings add to other studies[58–64] by delimiting in the same cohort the respective effects of social position and work environment on cancer risk. These distinct effects may be mediated by different risk factors such as sleep disorders in the case of bad work environment or smoking in the case of social position. The finding that unemployment exposure is not associated with the prevalence of any type of cancers is in disagreement with results from previous studies.[29, 32] This discrepancy might arise from the absence of adjustment for work environment in these studies, leaving the possibility that the observed increase in the prevalence of some types of cancers would be related to bad work environment rather than unemployment.

It is interesting to note that social position, work environment and unemployment duration remain associated with the prevalence of cardiovascular events and cancers even after adjustment for risk factors, suggesting that they would increase cardiovascular and cancer risks not only by overexposure to risk factors but also through other pathways yet to be defined. Identifying these pathways may not be so easy as the potential stressful effects of social position, work environment and unemployment duration are numerous and entangled.

The present study has several limitations. First, the external validity of the findings is not

guaranteed given that they were obtained in a cohort of participants which was not representative of the French population. Second, occupational and social data as well as health status were self-reported and may therefore have been imprecise, despite the fact that the information on health status was collected by a physician. Third, as a consequence of self-reporting, information on the occurrence of fatal cardiovascular events and cancers was not available and the diagnosis of these pathologies was relatively simple with no distinction for example between ischemic and hemorrhagic strokes or between the different types of skin cancers. Fourth, social position and work environment were assessed at the time of the inclusion and may have not reflected the conditions in which participants lived during most of their lifetime, even though a complete disconnection is unlikely. Finally, due to the cross-sectional and retrospective design of the analyses, reverse causation cannot be ruled out but it is difficult to imagine how early occurrence of cardiovascular events and cancers could have strongly modified social position and created bad work environment for people benefiting from the protective French social security system. Likewise, reverse causation is unlikely for unemployment exposure given that the episodes occurred in average prior to the occurrence of cardiovascular events and cancers.

In conclusion, this study indicates that although low social position, bad work environment and

unemployment exposure are tightly interrelated, they are associated with distinct cardiovascular and cancerous outcomes that could add up during lifetime and should therefore be considered all together to optimally design preventive strategies.

Author contributions: MSR performed statistical analyses, data interpretation and critical revision of the manuscript for important intellectual content; MP, GA and NH were involved in study concept and design and performed critical revision of the manuscript for important intellectual content; CR, MG and MZ obtained cohort funding and performed critical revision of the manuscript for important intellectual content; PM supervised the study and wrote the first draft of the manuscript. PM confirms that he had full access to all the data and has final responsibility for the decision to submit for publication.

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011). Participants gave informed written consent to participate in the study.

Data availability statement: Personal health data underlying the findings of our study are not publicly available due to legal reasons related to data privacy protection. However, the data are available upon reasonable request after approval from the French National Data Protection Authority. The email address for any inquiry is contact@constances.fr.

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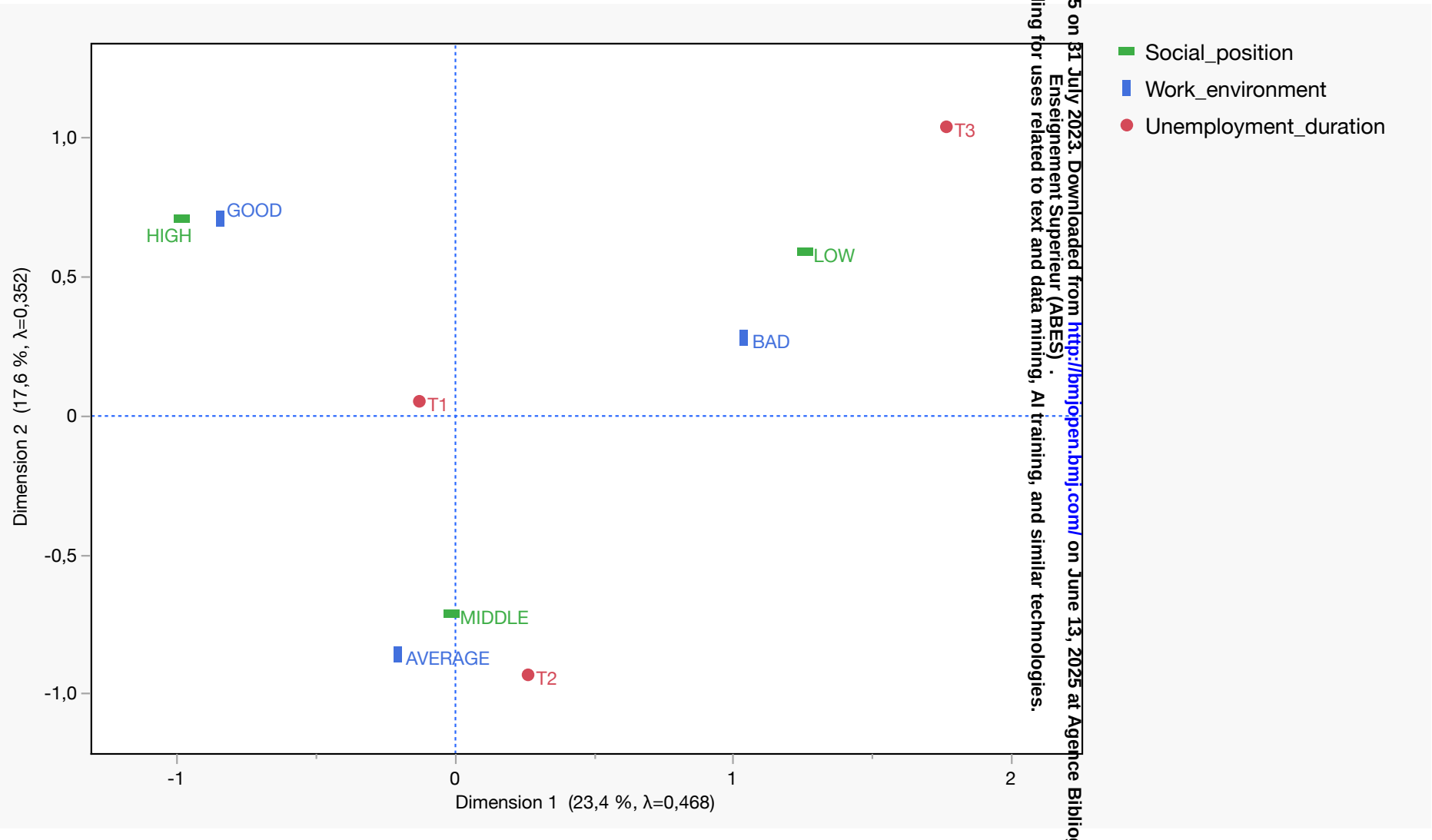
FIGURE CAPTION

Figure 1: Multiple correspondence analysis showing the association between social position, work environment and unemployment duration. The plot uses the two first dimensions which explain respectively 23.4 and 17.6% of the total inertia (81.7 and 1.6% with Greenacre adjustment).

Figure 2: Summary of the associations of social position, work environment and unemployment exposure with the prevalence of cardiovascular events and cancers after adjustment for risk factors. The putative directions of the associations are represented by arrows.



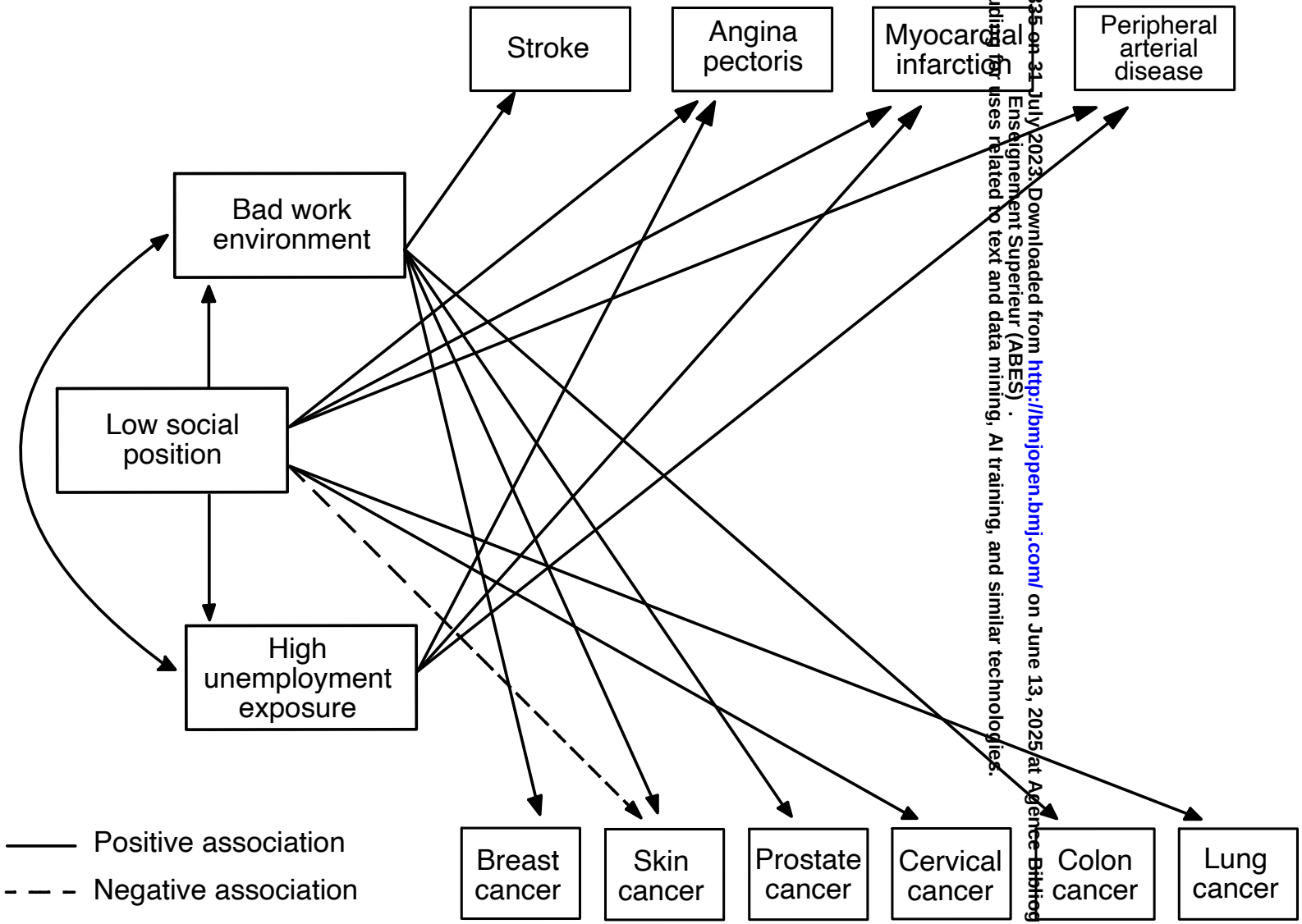


Table S1: Characteristics of cohort participants with or without missing values compared to randomly selected individuals from the French population.

		Representative sample of the French population		Whole cohort		Cohort without missing value		Comparing representative sample of the French population and whole cohort	Comparing representative sample of the French population and cohort without missing value	Comparing whole cohort and cohort without missing value
		n	%	n	%	n	%	Cohen's h	Cohen's h	Cohen's h
-	**All**	24,242	-	205,203	-	130,197	-	-	-	-
Sex	**Women**	12,745	52.6	110,193	53.7	66,743	51.3	-0.022	0.026	0.048
	Men	11,497	47.4	95,010	46.3	63,454	48.7	0.022	-0.026	-0.048
Age (y)	**18-39**	9657	39.9	66,832	32.6	46,892	36.0	0.152	0.080	-0.072
	40-54	7717	31.8	69,100	33.6	43,443	33.4	-0.038	-0.034	0.004
	55-75	6868	28.4	69,271	33.8	39,862	30.6	-0.117	-0.048	0.069
Education	**University**	6022	24.9	118,646	58.9	82,930	64.2	-0.705**	0.814***	-0.109
	Secondary school	11,643	48.0	33,246	16.5	20,748	16.1	0.694**	0.705**	0.011
	Primary school	6577	27.1	49,538	24.6	25,431	19.7	0.057	0.175	0.118
Occupation	**Management**	3103	15.5	58,441	32.2	42,099	35.8	-0.398*	-0.474*	-0.076
	Intermediate	5060	25.2	54,114	29.9	35,885	30.6	-0.105	-0.121	-0.015
	Blue collar/clerk	11,900	59.3	68,817	37.9	39,505	33.6	0.432*	0.521**	0.090

The percentages were calculated relatively to the number of cohort participants with or without missing values or of individuals randomly selected from the French population; Each pair of proportions was compared using Cohen's h, measure of effect size with the rule of thumb to categorize substantial differences as *small ($0.2 \leq h < 0.5$), **medium ($0.5 \leq h > 0.8$) ; ***large ($h \geq 0.8$).

Table S2: Indicators of social position of participants at inclusion.

		n	%
Education (y)	**≥17**	35,557	27.5
	14-16	47,373	36.7
	12-13	20,748	16.1
	≤11	25,431	19.7
Occupation	**Management**	42,099	35.8
	Intermediate	35,885	30.6
	Blue collar/clerk	39,505	33.6
Income	**Very high**	39,952	32.6
	High	40,396	32.9
	Middle	31,339	25.5
	Low	11,019	9.0
Spouse occupation	**Management**	32,048	34.7
	Intermediate	25,037	27.1
	Blue collar/clerk	35,268	38.2
Social vulnerability	**Low**	40,116	30.9
	Average	45,849	35.4
	High	43,729	33.7

The percentages were calculated relatively to the total number of participants in the cohort.

Figure S1: Multiple correspondence analysis showing the association between the different indicators used to characterize social position of participants at inclusion. The plot uses the two first dimensions which explain respectively 18.3 and 11.7% of the total inertia (60% and 8.9% with Greenacre adjustment).

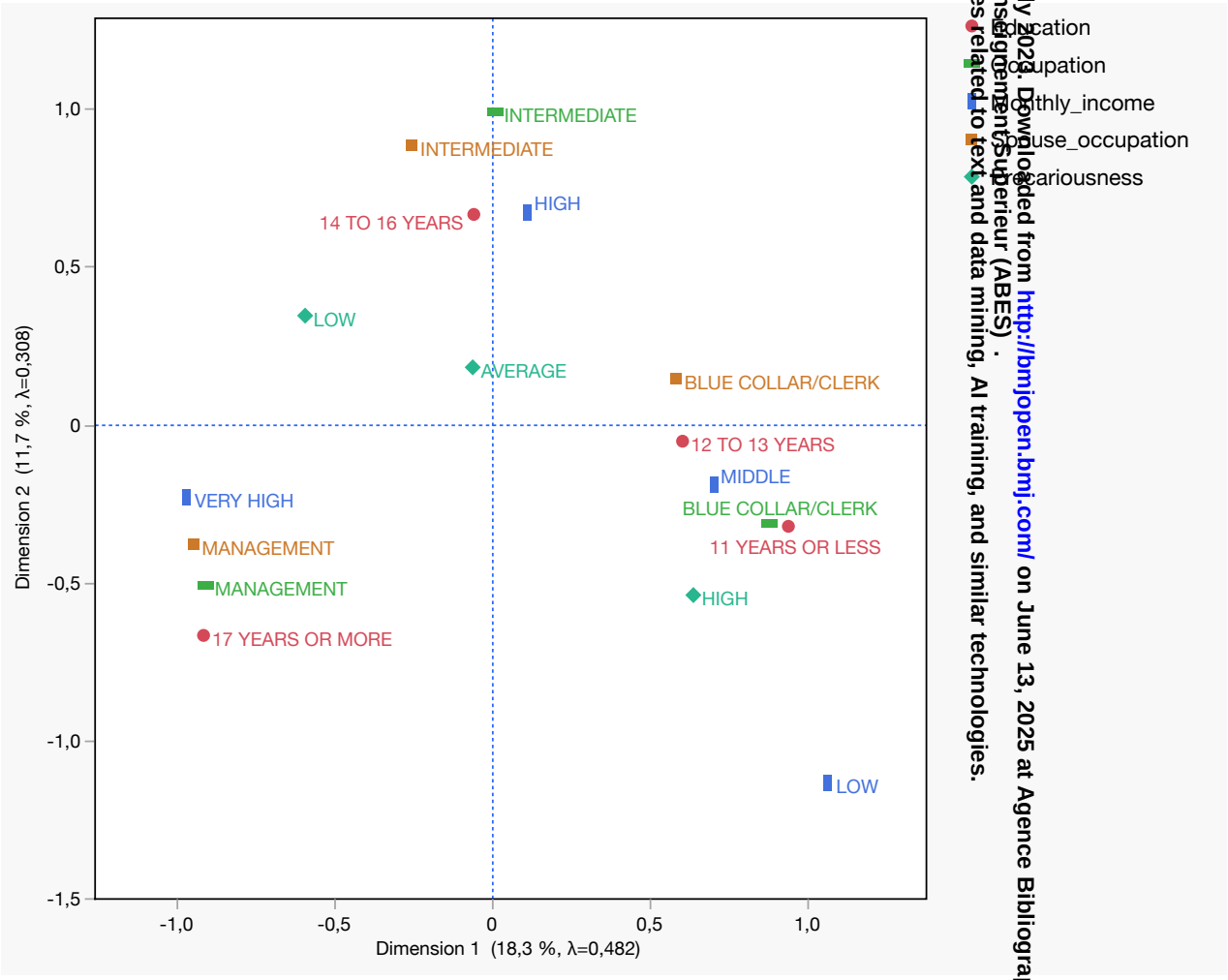


Table S3: Indicators of work environment of participants at inclusion.

		n	%
Commuting time	**<1h**	72,604	76.4
	1h-2h	18,757	19.7
	>2h	3648	3.9
Clocking in and out	**No**	74,281	77.8
	Yes	21,186	22.2
Regular working hours	**No**	53,085	55.4
	Yes	42,755	44.6
Long working hours	**No**	91,576	70.3
	Yes	38,621	29.7
Night work	**No**	118,011	90.6
	Yes	12,186	9.4
Dealing with the public	**No**	47,177	71.5
	Yes	18,801	28.5
Driving on public road	**No**	84,666	88.1
	Yes	11,397	11.9
Repetitive work	**No**	71,866	76.2
	Yes	22,401	23.8
Working with a screen	**No**	22,353	23.4
	Yes	73,266	76.6
Standing work posture	**No**	50,917	52.9
	Yes	45,246	47.1
Handling heavy loads	**No**	59,662	62.3
	Yes	36,112	37.7
Physically demanding work	**No**	93,933	72.2
	Yes	36,264	27.8
Exposure to vibrations	**No**	91,992	96.6
	Yes	3290	3.4
Exposure to noise	**No**	92,000	70.7
	Yes	38,197	29.3
Outdoor work	**No**	87,810	90.2
	Yes	9492	9.8
Working in the cold	**No**	93,155	96.8
	Yes	3075	3.2
Working in the heat	**No**	92,140	95.6
	Yes	4257	4.4
Exposure to chemicals	**No**	86,472	66.4
	Yes	43,725	33.6
Effort-reward imbalance	**Low**	30,381	31.8
	Average	36,199	37.9
	High	28,940	30.3

The percentages were calculated relatively to the total number of participants in the cohort.

Figure S2: Multiple correspondence analysis showing the association between the different occupational exposures used to characterize work environment of participants at inclusion. The plot uses the two first dimensions which explain respectively 16.8 and 12.0% of the total inertia (43.5 and 17.8% with Greenacre adjustment).

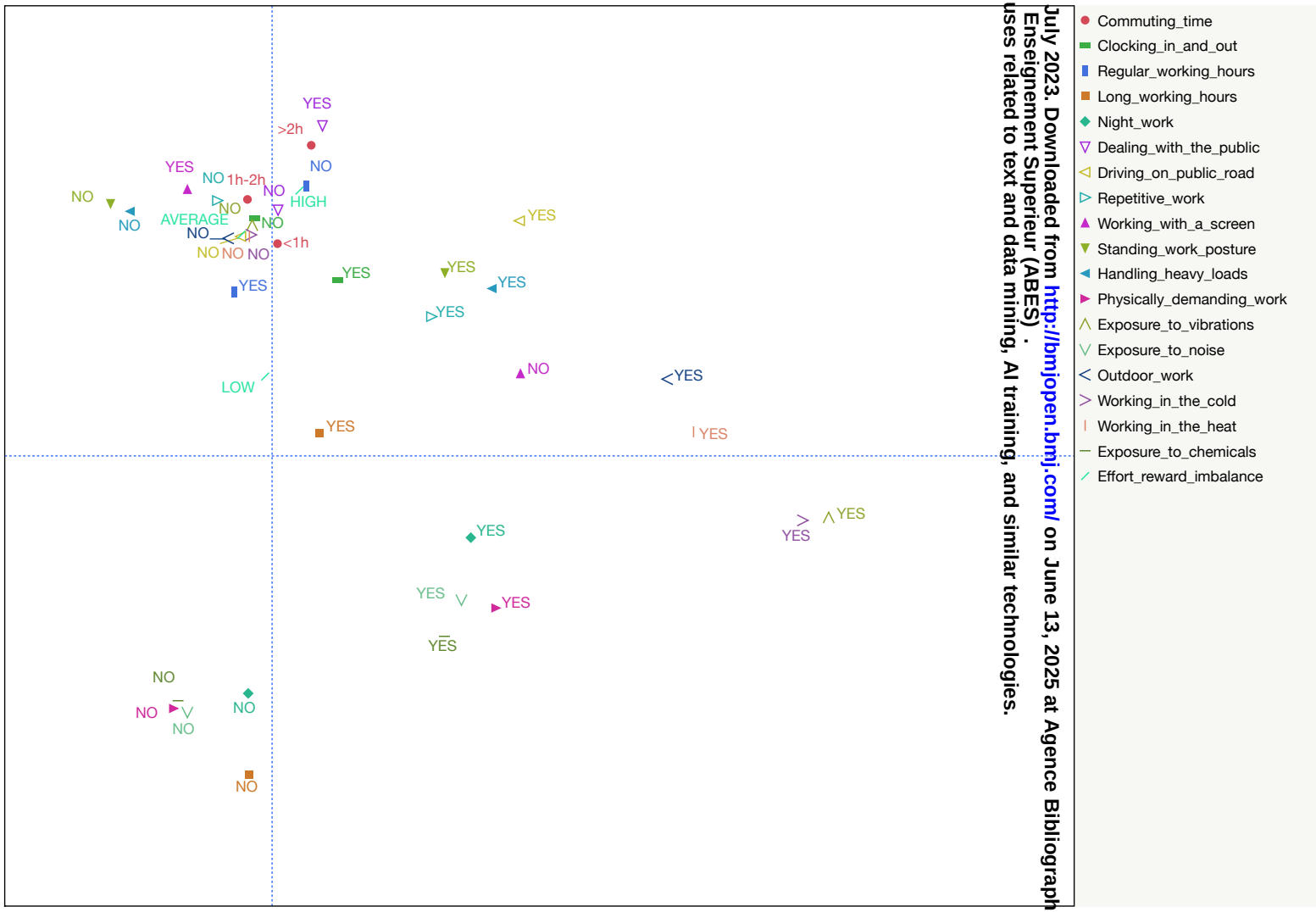


Table S4: Adjusted odds ratios (95% confidence interval, p) for the prevalence of cardiovascular events or cancers in participants at inclusion according to their exposure to common risk factors.

		Cardiovascular event		Cancer	
Sex	**Women**	1.00		1.00	
	Men	2.32 (2.09-2.58)	<0.0001	0.61 (0.58-0.65)	<0.0001
Age (y)	**18-39**	1.00		1.00	
	40-54	3.17 (2.50-4.02)	<0.0001	3.30 (2.94-3.70)	<0.0001
	55-75	6.72 (5.34-8.46)	<0.0001	8.60 (7.70-9.61)	<0.0001
Parental history of cardiovascular event	**No**	1.00		1.00	
	Yes	1.31 (1.20-1.44)	<0.0001	0.97 (0.92-1.03)	0.39
Parental history of cancer	**No**	1.00		1.00	
	Yes	0.94 (0.86-1.03)	0.21	1.28 (1.22-1.35)	<0.0001
Lifetime non-moderate alcohol consumption	**Rarely**	1.00		1.00	
	Sometimes	0.95 (0.80-1.12)	0.51	0.99 (0.91-1.09)	0.95
	Often	0.90 (0.78-1.03)	0.12	0.94 (0.87-1.02)	0.12
Smoking	**Never**	1.00		1.00	
	Former	1.48 (1.34-1.63)	<0.0001	1.10 (1.04-1.17)	0.001
	Current	1.37 (1.19-1.57)	<0.0001	0.85 (0.78-0.92)	0.0002
Leisure-time physical inactivity	**No**	1.00		1.00	
	Yes	1.09 (0.94-1.27)	0.24	1.00 (0.91-1.11)	0.93
Body mass index	**Optimal**	1.00		1.00	
	Overweight	1.05 (0.94-1.16)	0.39	0.95 (0.89-1.01)	0.09
	Obesity	0.99 (0.87-1.12)	0.83	0.93 (0.85-1.01)	0.09
Hypertension	**No**	1.00		1.00	
	Yes	2.17 (1.96-2.39)	<0.0001	1.05 (0.97-1.24)	0.19
Dyslipidemia	**No**	1.00		1.00	
	Yes	5.89 (5.34-6.49)	<0.0001	1.07 (0.98-1.37)	0.11
Diabetes	**No**	1.00		1.00	
	Yes	1.11 (0.94-1.31)	0.20	1.11 (0.94-1.30)	0.22
Sleep disorders	**No**	1.00		1.00	
	Yes	1.15 (1.05-1.26)	0.003	1.16 (1.09-1.23)	<0.0001
Depression	**No**	1.00		1.00	
	Yes	1.29 (1.14-1.46)	<0.0001	1.09 (1.01-1.18)	0.03

Models were adjusted for sex, age, parental history of cardiovascular event, parental history of cancer, social position, work environment, unemployment duration, lifetime non-moderate alcohol consumption, smoking, leisure-time physical inactivity, body mass index, hypertension, dyslipidemia, diabetes, sleep disorders and depression.

Table S5: Adjusted odds ratios (95% confidence interval) for the prevalence of specific non-fatal cancers in participants at inclusion according to unemployment duration.

Body location	Unemployment duration (quarters)	n	%	Models 1	p	Models 2	p	Models 3	p
All	0	5018	4.50	1.00		1.00		1.00	
	1-19	532	4.19	0.95 (0.86-1.04)	0.25	0.95 (0.87-1.04)	0.37	0.95 (0.87-1.05)	0.31
	20-148	380	6.24	0.98 (0.88-1.09)	0.71	0.96 (0.86-1.07)	0.47	0.96 (0.86-1.07)	0.44
Breast	0	1300	1.17	1.00		1.00		1.00	
	1-19	162	1.28	1.02 (0.86-1.21)	0.80	1.04 (0.88-1.23)	0.66	1.03 (0.87-1.22)	0.73
	20-148	128	2.10	1.03 (0.85-1.24)	0.79	1.02 (0.84-1.23)	0.86	1.01 (0.83-1.22)	0.94
Skin	0	1267	1.14	1.00		1.00		1.00	
	1-19	129	1.02	0.92 (0.76-1.10)	0.35	0.95 (0.79-1.13)	0.62	0.96 (0.80-1.15)	0.67
	20-148	69	1.13	0.72 (0.56-0.92)	0.009	0.77 (0.60-0.98)	0.03	0.78 (0.61-1.01)	0.06
Prostate	0	611	0.55	1.00		1.00		1.00	
	1-19	39	0.31	0.72 (0.52-1.00)	0.05	0.75 (0.54-1.04)	0.09	0.76 (0.55-1.06)	0.11
	20-148	34	0.56	0.92 (0.65-1.31)	0.65	0.91 (0.64-1.29)	0.59	0.94 (0.66-1.33)	0.71
Cervical	0	254	0.23	1.00		1.00		1.00	
	1-19	38	0.30	1.19 (0.85-1.68)	0.31	1.15 (0.81-1.61)	0.44	1.11 (0.78-1.56)	0.56
	20-148	33	0.54	1.54 (1.07-2.22)	0.02	1.36 (0.94-1.97)	0.10	1.26 (0.87-1.83)	0.22
Colon	0	259	0.23	1.00		1.00		1.00	
	1-19	33	0.26	1.22 (0.85-1.76)	0.28	1.24 (0.86-1.79)	0.24	1.23 (0.85-1.78)	0.26
	20-148	19	0.31	0.95 (0.60-1.52)	0.84	0.92 (0.57-1.47)	0.71	0.92 (0.57-1.47)	0.72
Thyroid	0	270	0.24	1.00		1.00		1.00	
	1-19	36	0.28	1.12 (0.79-1.59)	0.52	1.10 (0.78-1.56)	0.59	1.11 (0.78-1.57)	0.57
	20-148	19	0.31	0.89 (0.56-1.43)	0.64	0.84 (0.53-1.35)	0.48	0.87 (0.54-1.40)	0.56
Lymphoma	0	263	0.24	1.00		1.00		1.00	
	1-19	23	0.18	0.79 (0.52-1.22)	0.29	0.79 (0.52-1.21)	0.28	0.79 (0.51-1.21)	0.27
	20-148	18	0.30	1.11 (0.68-1.79)	0.67	1.08 (0.67-1.76)	0.75	1.07 (0.66-1.74)	0.78
Lung	0	69	0.06	1.00		1.00		1.00	
	1-19	4	0.03	0.56 (0.20-1.54)	0.26	0.53 (0.19-1.45)	0.22	0.50 (0.18-1.38)	0.18
	20-148	5	0.08	1.08 (0.43-2.68)	0.87	0.92 (0.37-2.30)	0.86	0.84 (0.33-2.11)	0.71

The percentages were calculated relatively to the number of participants for each unemployment duration (0 quarter=111,407; 1-19 quarters=12,702; 20-148 quarters=6088).

Models 1 were adjusted for sex, age and parental history of cancer.

Models 2 were adjusted for sex, age, parental history of cancer, social position and work environment.

Models 3 were adjusted for sex, age, parental history of cancer, work environment, unemployment duration, lifetime non-moderate alcohol consumption, smoking, body mass index and sleep disorders.

Figure S3: Age differences between the occurrence of unemployment episodes, cardiovascular events and cancers during the lifetime of participants. The mean age at which each cardiovascular event or cancer occurred was compared to the mean age at which unemployment episodes happened. In each box plot, the horizontal line represents the median value, the ends and the length of the box represent the 1st and 3rd quartiles and the interquartile range (IR) respectively, the lines from each end of the box extend to the outermost values that fall within 1st quartile -1.5*IR and 3rd quartile + 1.5*IR, values outside this interval are presented as individual points. The differences were assessed with the non-parametric Wilcoxon-Mann-Whitney test. *** p<0.0001.

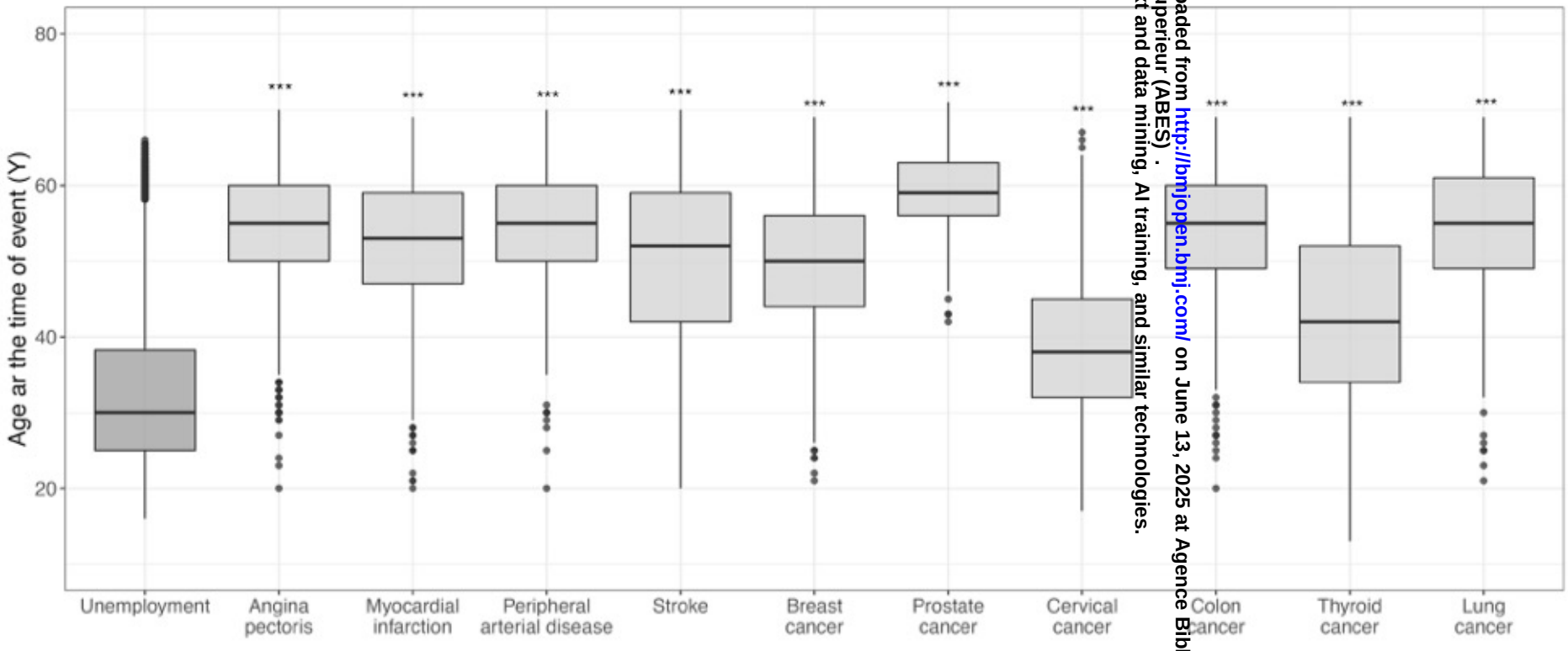


Table S6: Multi-adjusted odds ratios (95% confidence interval) for the prevalence of non-fatal cardiovascular events in men and women at inclusion according to their social position, work environment and unemployment exposure.

		Type of event	Men		Women	
			OR	p	OR	p
Social position	High	All	1.00		1.00	
	Middle		1.14 (0.98-1.32)	0.08	1.05 (0.83-1.34)	0.66
	Low		1.29 (1.10-1.51)	0.002	1.24 (0.95-1.62)	0.11
	High	Stroke	1.00		1.00	
	Middle		1.03 (0.80-1.32)	0.81	0.96 (0.73-1.27)	0.80
	Low		1.20 (0.91-1.57)	0.19	0.97 (0.70-1.34)	0.84
	High	Angina pectoris	1.00		1.00	
	Middle		1.17 (0.91-1.49)	0.22	2.26 (1.17-4.37)	0.01
	Low		1.20 (0.92-1.56)	0.18	3.45 (1.73-6.91)	0.0005
	High	Myocardial infarction	1.00		1.00	
	Middle		1.11 (0.88-1.39)	0.39	0.79 (0.47-1.33)	0.37
	Low		1.27 (1.00-1.61)	0.05	0.81 (0.45-1.47)	0.49
	High	Peripheral arterial disease	1.00		1.00	
	Middle		1.36 (0.84-2.20)	0.22	0.91 (0.44-1.90)	0.80
	Low		2.19 (1.35-3.55)	0.002	1.47 (0.66-3.27)	0.35
Work environment	Good	All	1.00		1.00	
	Average		0.89 (0.74-1.06)	0.20	0.99 (0.77-1.27)	0.94
	Bad		1.24 (1.06-1.46)	0.009	1.25 (0.99-1.59)	0.06
	Good	Stroke	1.00		1.00	
	Average		0.93 (0.69-1.26)	0.65	0.95 (0.71-1.28)	0.76
	Bad		1.25 (0.95-1.65)	0.11	1.21 (0.90-1.61)	0.20
	Good	Angina pectoris	1.00		1.00	
	Average		0.76 (0.56-1.03)	0.08	0.97 (0.56-1.68)	0.90
	Bad		1.11 (0.85-1.44)	0.44	1.04 (0.63-1.74)	0.87
	Good	Myocardial infarction	1.00		1.00	
	Average		0.99 (0.75-1.31)	0.97	0.83 (0.47-1.43)	0.49
	Bad		1.21 (0.94-1.55)	0.14	0.81 (0.48-1.37)	0.43
	Good	Peripheral arterial disease	1.00		1.00	
	Average		0.93 (0.53-1.61)	0.79	0.80 (0.38-1.65)	0.54
	Bad		1.32 (0.82-2.14)	0.26	0.86 (0.42-1.75)	0.68
Unemployment duration (quarters)	0	All	1.00		1.00	
	1-19		1.05 (0.87-1.26)	0.60	0.83 (0.60-1.13)	0.23
	20-148		1.55 (1.27-1.88)	<0.0001	1.16 (0.86-1.56)	0.33
	0	Stroke	1.00		1.00	
	1-19		0.85 (0.60-1.21)	0.38	0.84 (0.57-1.22)	0.36
	20-148		1.18 (0.82-1.72)	0.37	1.06 (0.71-1.57)	0.79
	0	Angina pectoris	1.00		1.00	
	1-19		1.06 (0.78-1.45)	0.70	0.98 (0.54-1.81)	0.96
	20-148		1.77 (1.30-2.40)	0.0003	0.69 (0.33-1.45)	0.33
	0	Myocardial infarction	1.00		1.00	
	1-19		1.16 (0.88-1.51)	0.29	0.88 (0.42-1.84)	0.74
	20-148		1.58 (1.19-2.10)	0.002	1.92 (1.06-3.49)	0.03
	0	Peripheral arterial disease	1.00		1.00	
	1-19		1.15 (0.72-1.86)	0.55	0.88 (0.35-2.24)	0.79
	20-148		1.89 (1.21-2.97)	0.005	1.31 (0.54-3.18)	0.54

Logistic regression models included social position, work environment and unemployment duration and were adjusted for age, parental history of cardiovascular event, lifetime non-moderate alcohol consumption, smoking, leisure-time physical inactivity, body mass index, hypertension, dyslipidemia, diabetes, sleep disorders and depression.

Table S7: Multi-adjusted odds ratios (95% confidence interval) for the prevalence of non-fatal cancers in men and women at inclusion according to their social position and work environment.

		Body location	Men		Women	
			OR	p	OR	p
Social position	High	All	1.00		1.00	
	Middle		0.90 (0.81-1.01)	0.07	1.02 (0.94-1.12)	0.59
	Low		0.81 (0.72-0.92)	0.001	1.10 (0.99-1.23)	0.08
	High	Breast	N/A		1.00	
	Middle				0.94 (0.82-1.07)	0.37
	Low				0.97 (0.83-1.13)	0.71
	High	Skin	1.00		1.00	
	Middle		0.76 (0.63-0.91)	0.004	0.91 (0.76-1.08)	0.28
	Low		0.59 (0.47-0.75)	<0.0001	0.78 (0.63-0.98)	0.03
	High	Prostate	1.00		N/A	
	Middle		0.92 (0.74-1.14)	0.44		
	Low		0.84 (0.67-1.06)	0.14		
	High	Cervical	N/A		1.00	
	Middle				1.37 (1.01-1.86)	0.04
	Low				1.72 (1.21-2.45)	0.002
	High	Colon	1.00		1.00	
	Middle		1.68 (1.08-2.63)	0.02	0.75 (0.47-1.19)	0.22
	Low		1.17 (0.70-1.95)	0.54	1.22 (0.75-1.98)	0.43
	High	Thyroid	1.00		1.00	
	Middle		1.56 (0.84-2.89)	0.16	1.18 (0.84-1.65)	0.33
	Low		1.41 (0.67-3.00)	0.37	1.38 (0.94-2.04)	0.10
	High	Lymphoma	1.00		1.00	
	Middle		1.07 (0.72-1.59)	0.75	1.28 (0.81-2.02)	0.30
	Low		1.04 (0.65-1.68)	0.86	1.25 (0.72-2.17)	0.43
	High	Lung	1.00		1.00	
	Middle		1.14 (0.51-2.57)	0.75	0.99 (0.30-3.31)	0.99
	Low		1.73 (0.74-4.03)	0.20	1.94 (0.56-6.69)	0.29
Work environment	Good	All	1.00		1.00	
	Average		0.88 (0.76-1.01)	0.07	0.99 (0.90-1.09)	0.79
	Bad		1.75 (1.54-1.98)	<0.0001	1.36 (1.24-1.49)	<0.0001
	Good	Breast	N/A		1.00	
	Average				0.94 (0.81-1.09)	0.41
	Bad				1.29 (1.13-1.48)	0.0002
	Good	Skin	1.00		1.00	
	Average		0.99 (0.78-1.27)	0.98	0.88 (0.72-1.06)	0.18
	Bad		1.58 (1.26-1.98)	<0.0001	1.25 (1.03-1.50)	0.02
	Good	Prostate	1.00		N/A	
	Average		0.68 (0.46-1.01)	0.06		
	Bad		3.02 (2.29-3.99)	<0.0001		
	Good	Cervical	N/A		1.00	
	Average				0.95 (0.70-1.27)	0.71
	Bad				1.17 (0.87-1.58)	0.28
	Good	Colon	1.00		1.00	
	Average		0.73 (0.41-1.30)	0.29	1.67 (0.94-2.97)	0.08
	Bad		1.74 (1.08-2.79)	0.02	2.50 (1.48-4.22)	0.0006
	Good	Thyroid	1.00		1.00	
	Average		0.96 (0.50-1.82)	0.89	1.21 (0.86-1.70)	0.27
	Bad		0.87 (0.44-1.71)	0.68	1.28 (0.90-1.81)	0.17
	Good	Lymphoma	1.00		1.00	
	Average		0.69 (0.44-1.09)	0.11	0.82 (0.53-1.29)	0.40
	Bad		0.96 (0.63-1.48)	0.87	1.11 (0.71-1.76)	0.64
	Good	Lung	1.00		1.00	
	Average		1.62 (0.61-4.24)	0.33	0.54 (0.16-1.86)	0.33
	Bad		1.54 (0.60-3.96)	0.37	1.02 (0.38-2.75)	0.97

Logistic regression models included social position, work environment and unemployment duration and were adjusted for age, parental history of cancer, lifetime non-moderate alcohol consumption, smoking, body mass index and sleep disorders. NA: non applicable.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	
Objectives	3	State specific objectives, including any prespecified hypotheses	5	
Methods				
Study design	4	Present key elements of study design early in the paper		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	thru 11	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	thru 11	
Bias	9	Describe any efforts to address potential sources of bias	6 & 10	
Study size	10	Explain how the study size was arrived at	6	

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11 & 12
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11 & 12
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	6
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	13 & 14
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	15 thru 20
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15 thru 20
		(*b*) Report category boundaries when continuous variables were categorized	15 thru 20
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	22 & 23
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	24
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	24
Generalisability	21	Discuss the generalisability (external validity) of the study results	24
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. Information on the STROBE Initiative is available at www.strobe-statement.org.