# Investigating the spatial variability in incidence of coronary heart disease in the Gazel cohort: the impact of area socioeconomic position and mediating role of risk factors.

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**Investigating the spatial variability in incidence of coronary heart disease in the Gazel**

**Cohort: the impact of area socioeconomic position and mediating role of risk factors**

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**Abstract**:

**Study objective:** The study aim was to improve our understanding of the relationships between contextual socioeconomic characteristics and coronary heart disease (CHD) incidence in France. Several authors have suggested that CHD risk factors (diabetes, hypertension, cholesterol, overweight, tobacco consumption) may partly mediate associations between socioeconomic environmental variables and CHD. However, studies have assessed the overall mediating role of CHD risk factors, but have never investigated the specific mediating role of each risk factor, not allowing disentangling their specific contribution to the area socioeconomic position–CHD association.

   **Design:** After assessing geographical variations in CHD incidence and socioeconomic environmental effects on CHD using a multilevel Cox model, we assessed the extent to which this contextual effect was mediated by each of the CHD risk factors.

   **Participants:** We used data of the French GAZEL cohort (n = 19808).

   **Main results:** After adjustment for several individual socioeconomic indicators, we found, among men from highly urbanized environments, that CHD incidence increased with decreasing socioeconomic position of the residential environment. After individual-level adjustment, a higher risk of obesity, smoking, and cholesterol was observed in the most deprived residential environments. When risk factors were introduced into the model, we observed a modest decrease in the magnitude of the association between the socioeconomic contextual variable and CHD. Risk factors that contributed most to the decrease of the association were smoking and cholesterol.

   **Conclusions:** Classical risk factors, though some of them more than others, mediated a modest part of the association between area socioeconomic position and CHD.


**Keywords:** ischaemic heart disease; residential context; socioeconomic factors

There is growing evidence that the social determinants of disease risk can intervene both at the individual level and at the level of different life contexts (residential environment, workplace environment, etc.).[1][2] Contextual studies, investigating the influence of the residential environment on health, may be useful to develop efficient policies through a better targeting of populations with a higher risk of diseases and a better understanding of mechanisms producing health disparities. For example, studies have shown that neighbourhood socioeconomic characteristics can influence tobacco use,[3][4] physical activity[5] and mortality,[6] independently of the effects of individual socioeconomic characteristics.

The association between individual socioeconomic factors and incidence of coronary heart disease (CHD) has been extensively investigated in previous literature.[7] It has also been shown that incidence of and mortality by CHD varies across space.[8] Such geographical variations between and within large regions remain largely unexplained, which has led researchers to study contextual effects operating on different scales.[9] Several studies have shown associations between socioeconomic contextual characteristics and incidence of CHD or mortality by CHD.[2][10][11][12][13][14][15][16] However, no study to date has tested this specific hypothesis in France, not permitting to assess whether CHD risk also depends on the poverty level of the residential environment in the French context.

A limitation of current literature is that it does not allow understanding the mechanisms through which the area socioeconomic environment may influence coronary health. A commonly evoked hypothesis is that classical CHD risk factors may intervene as mediators in these associations. It has been shown that the spatial distribution of CHD risk factors (physical inactivity, overweight, tobacco consumption, hypertension, cholesterol) is shaped by individuals' residential environment, including its socioeconomic characteristics.[5][17]

3

The present study had three objectives: first, to quantify the magnitude of geographic variability in CHD incidence, attempting to determine the spatial scale on which variations were operating; second, to estimate associations between socioeconomic contextual factors and CHD incidence, after controlling for the sociodemographic characteristics of individuals; third, to examine the extent to which the association between area socioeconomic position and CHD was mediated by each of the classical cardiovascular risk factors (diabetes, hypertension, cholesterol, overweight, and tobacco consumption).

**Methods**

**Population**

In the present study, we used the data of the GAZEL cohort.[18][19][20] There were 20 542 women and men at baseline in 1989. Women (27% of the sample) were 35 to 50 year old, and men were 40 to 50 year old at baseline. All the participants were working for the companies EDF (Electricity of France) and GDF (Gas of France) and were volunteer to participate. They all receive an annual questionnaire since 1989, which investigates participants' physical and mental health, health behaviours, and other issues. Occupational and personal data are updated through human resources department files. Information on incidence of coronary heart diseases was obtained from the company's Health Insurance Department.[21][22]

We combined different datasets at the individual level:
- a demographic database including the age, gender, dates of death or retirement, and municipality of residence of individuals in 1990;
- data from the 1989 and 1990 auto-questionnaires containing information on household composition, household income, educational attainment of individuals, weight, height,

tobacco consumption, cholesterol, hypertension, diabetes, and prevalent common chronic

conditions assessed from a checklist.

- a dataset on the occupational trajectory of individuals;

- a dataset reporting the incident cases of CHD from January 1st 1990 to December 31st 2000

and their nature (angina pectoris, acute myocardial infection, sudden death); people who

stopped answering to the annual questionnaires over the study period were nevertheless

followed in this register, but those who retired were no longer followed.

We excluded the following participants from our database: those for whom the

occupation was unknown [N = 501], those who had had a CHD event before January 1st 1990

[N = 37], those from the French overseas territories [N = 136], and those with a missing or

inadequate municipality code [N = 66]. Our final database includes 19 808 participants. We

used the 1990 French census to determine characteristics of residential municipalities.

**Measures**

In this study, the main outcome variable was incidence of CHD. For each individual, we only

considered the first incident event (only 4% of the participants with an incident CHD had had

more than one event).

As explanatory variables, we took into account both individual characteristics and area

characteristics. We considered age as a continuous variable. Educational attainment was

coded in two classes: (i) people who completed secondary school or had a university degree

and (ii) those who did not. Regarding baseline occupation,[23] a categorisation from the

French National Institute of Statistics and Economic Studies (INSEE) allowed us to

distinguish between high white-collar workers, intermediate occupation, and low white- and

blue-collar workers. Household income was divided by the number of consumption units, and

categorised into three classes. Marital status was coded in two classes: alone (single, divorced, or widowed) or not (married or in couple).

Regarding CHD risk factors, smoking was coded in four classes: non-smokers, previous-smokers, light-to-moderate smokers (20 cigarettes per day or less), and hard smokers (more than 20 cigarettes). Body mass index (BMI) was defined as self-reported weight (in kg) divided by the square of self-reported height (in m). Overweight corresponds to a BMI between 25 and 30, and obesity to a BMI greater than 30. We also constituted 3 binary variables based on questions asking to the participants whether they suffered from diabetes, hypertension, or cholesterol.

Using the 1990 census, we defined two contextual variables at the municipality level, i.e., the percentage of chief executive officers (CEO) of companies comprising 10 employees or more among inhabitants aged 25 to 60 years, and the percentage of inhabitants aged 25 to 60 years who had a university degree or equivalent. The percentage of CEOs was selected on the basis of the *a priori* argument that CEOs are among those who have no financial constraint when choosing their residential environment; thus the area percentage of CEOs may constitute a particularly accurate proxy of desirable, high-social status, and advantaged areas. The two area variables were divided in four classes comprising a similar number of GAZEL participants (cutoffs were redefined in each specific sample).

**Statistical analysis**

To quantify the geographical variability in CHD incidence and estimate individual and contextual effects on the incidence of the disease, we estimated multilevel Cox models. The multilevel Cox model can be written as:

$$\lambda(t, j) = \lambda_0(t) \exp(\beta X + u_{0j}) \text{ with } u_{0j} \sim N(0, \sigma_{u0}^2)$$

where X corresponds to a vector of explanatory variables and $u_{0j}$ to the area-level random effect for area j. The model assumes that this area-level random effect follows a normal distribution, and estimates the variance $\sigma_{u0}^2$ of its distribution.[24]

To quantify geographic variations in CHD incidence, we first estimated an empty model (that did not include any explanatory variable except age and gender). Geographic variability was assessed with the variance of the area-level random effect.[25][26][27] We estimated separate two-level models (individuals nested within areas), considering different area subdivisions at the 2nd level of the hierarchy (municipalities, counties, and regions). There were 3235 municipalities represented in our database, 96 counties, and 22 regions. For the GAZEL participants, the median number of inhabitants in those areas were 6871, 472325, and 1919847, respectively. The median number of GAZEL participants in those areas were 3, 127, and 597, respectively. To assess spatial autocorrelation in CHD incidence, i.e., whether areas adjacent one to the other had a more similar incidence risk that areas located further apart on the territory, we computed the Moran's *I* statistic for the area-level residuals of the multilevel model.[28] In the absence of spatial autocorrelation, the Moran's I statistic has a small negative expectation when applied to regression residuals.[29] In comparing the 95% confidence interval with the value 0, we have therefore applied a conservative test.

After estimating a model for the whole database, we estimated separate empty models among people living in highly urban territories and people from territories with a lower urbanicity degree, in order to compare the geographical variability in those distinct territories. Based on a definition of the French Institute of Statistics and Economic Studies, highly urban territories corresponded to urban municipalities or groupings of interconnected urban municipalities of 100 000 inhabitants or more.

Individual characteristics (marital status, education, occupation, and income) were then introduced into the model to examine whether geographical variability in CHD incidence

was due to compositional effects related to those individual variables. Contextual factors were then introduced into the model, to estimate associations between contextual factors and CHD adjusted for individual variables.

To assess whether cardiovascular risk factors (diabetes, hypertension, cholesterol, overweight, and tobacco consumption) had a mediating role in the associations between contextual variables and CHD incidence, we first estimated separate multilevel logistic models with those risk factors as the outcomes.

As a rough approximation of the extent to which each specific CHD risk factor mediated part of the area–CHD association, we finally compared the socioeconomic contextual effect (adjusted for individual socioeconomic variables) before and after controlling for each specific risk factor separately. In this final analysis, the area variable was included as an ordinal variable taking values from 1 to 4. We determined the proportional change in the socioeconomic area effect when including each specific risk factor separately, allowing to assess the mediating role of each risk factor.

We used SAS[30] to perform the statistical analysis. Cox models were estimated with R.[31][32]


**Results**

In our sample (19 808 participants), there were 27% of women. Participants were 36 to 51 year old on January 1st 1990. Between January 1 1990 and December 31 2000, 325 participants (1.6%) had an incident CHD (angina pectoris, acute myocardial infarction, or sudden death), including 195 myocardial infarctions (0.9%).

Table 1: Characteristics of the GAZEL participants and socioeconomic characteristics of their residential municipality according to the urbanicity degree of municipality, GAZEL cohort, 1990–2000, men and women

|  | High urbanicity degree (n = 10303) | Intermediate or low urbanicity degree (n = 9505) | Full sample (n = 19808) | p |
|---|---|---|---|---|
| *Individual characteristics* |  |  |  |  |
| Age (in years) * | 44.7 | 44.8 | 44.7 | 0.15 |
| Women § | 33.5% | 20.5% | 27.3% | <0.0001 |
| Low educational level § | 67.2% | 78.1% | 72.4% | <0.0001 |
| High white-collar workers § | 27.9% | 17.3% | 22.8% | <0.0001 |
| Median monthly household income (in euros) | 985€ | 812€ | 902€ | <0.0001 |
| *Municipality characteristics* |  |  |  |  |
| Percentage of CEOs in the municipality ‡ | 0.7% | 0.6% | 0.7% | <0.001 |
| Percentage with a university degree in the municipality ‡ | 19.6% | 11.1% | 15.5% | <0.001 |

* Student test; § Khi-square test; ‡ Wilcoxon test (the test was performed at the individual level with the municipality variable attributed to each individual)

In our population, 0.3% of women had an incident CHD event (15 out of 5387), and 2.2% of men (310 out of 4096). As a consequence, most of the analyses were only conducted among men. Table 1 describes the socioeconomic characteristics of the participants according to the urbanicity degree of their municipality. Participants residing in high-urbanicity degree municipalities had a higher educational level, a higher occupational status, and a higher household income.

To assess geographic variability in CHD incidence, we estimated empty multilevel survival models for CHD incidence, adjusted for age and gender only (see Table 2). Because of sample size limitations, a statistically significant area-level variance was only observed on a regional scale, even if much higher point estimates were observed at the municipality level. Investigating further spatial variations in CHD on a regional scale, the Moran's I indicated that there was no spatial autocorrelation in the residuals of the model. Significant variations in

CHD incidence were observed between regions among high urbanicity participants (area-level variance = 0.125, p =0.008). In contrast, there was no variability at all among participants from intermediate or low urbanicity degree territories (area-level variance = 0.001, p =0.49). Accordingly, all the following analyses are conducted among men from municipalities with a high urbanicity degree (6852 men, 127 CHD incident events), using multilevel models with individuals nested within region.

Table 2: Variance of the area random effect estimated from separate two-level (individuals, areas) empty multilevel survival models for CHD incidence (adjusted for age and gender), GAZEL cohort, 1990-2000, men and women

|  | Full population | Intermediate or low urbanicity degree | High urbanicity degree |
|---|---|---|---|
| *Full sample* |  |  |  |
| Geographical scale |  |  |  |
| Municipality level | 0.235 (p=0.32) | 0.083 (p=0.43) | 0.262 (p=0.32) |
| County level | 0.048 (p=0.19) | 0.001 (p=0.45) | 0.132 (p=0.06) |
| Region level | 0.038 (p=0.04) | 0.001 (p=0.50) | 0.135 (p=0.003) |
| *Among males* |  |  |  |
| Geographical scale |  |  |  |
| Municipality level | 0.150 (p=0.39) | 0.021 (p=0.39) | 0.204 (p=0.370) |
| County level | 0.044 (p=0.21) | 0.001 (p=0.45) | 0.103 (p=0.110) |
| Region level | 0.040 (p=0.055) | 0.001 (p=0.49) | 0.125 (p=0.008) |

Individual sociodemographic characteristics were then included into the model for CHD incidence (among male residents of high-urbanicity degree municipalities). As seen in Table 3, CHD incidence increased with decreasing occupational status and decreasing educational attainment. CHD incidence was not associated with household income. After including individual sociodemographic characteristics, the between-region variance decreased by 38%.

Table 3: Associations between individual and municipality characteristics and CHD incidence (hazard ratios and 95% CI), GAZEL cohort, 1990-2000, men residing in high-urbanicity degree municipalities

| | Empty model | Model including socioeconomic characteristics | Model further including the municipality variable | Model further including risk factors |
|---|---|---|---|---|
| Age (unit = 5 years) | 3.15 (2.30 to 4.31) | 4.42 (3.15 to 6.20) | 4.48 (3.19 to 6.28) | 4.35 (3.08 to 6.12) |
| Occupation (vs. high white-collar workers) | | | | |
| Low white-collar workers | | 1.68 (1.04 to 2.70) | 1.62 (1.01 to 2.61) | 1.64 (1.01 to 2.64) |
| Blue-collar workers | | 1.82 (0.97 to 3.43) | 1.79 (0.95 to 3.35) | 1.79 (0.95 to 3.40) |
| Single (vs. married or cohabiting) | | 1.20 (0.68 to 2.13) | 1.20 (0.68 to 2.13) | 1.04 (0.58 to 1.87) |
| Low educational attainment | | 1.80 (1.13 to 2.85) | 1.71 (1.08 to 2.72) | 1.61 (1.01 to 2.55) |
| Income (vs. high income) | | | | |
| Medium income | | 1.09 (0.69 to 1.73) | 1.09 (0.69 to 1.72) | 1.05 (0.66 to 1.67) |
| Low income | | 1.34 (0.85 to 2.12) | 1.30 (0.82 to 2.06) | 1.26 (0.79 to 2.00) |
| Municipality percentage of CEOs (vs. 4th quartile) | | | | |
| 3rd quartile | | | 1.10 (0.66 to 1.83) | 1.05 (0.63 to 1.76) |
| 2nd quartile | | | 1.39 (0.86 to 2.27) | 1.36 (0.84 to 2.22) |
| 1st quartile | | | 1.74 (1.08 to 2.79) | 1.58 (0.98 to 2.56) |
| BMI (vs. below 25) | | | | |
| Between 25 and 30 | | | | 1.21 (0.84 to 1.76) |
| Greater than 30 | | | | 1.94 (1.08 to 3.51) |
| Smoking (vs. non-smokers) | | | | |
| Former smokers | | | | 1.21 (0.77 to 1.89) |
| Light to moderate smokers | | | | 1.77 (1.08 to 2.90) |
| Hard smokers | | | | 2.79 (1.77 to 4.40) |
| Diabetes | | | | 2.08 (0.88 to 4.91) |
| Hypertension | | | | 1.58 (1.04 to 2.40) |
| Cholesterol | | | | 2.27 (1.56 to 3.29) |
| Area-level variance (p-value) | 0.125 (p=0.008) | 0.077 (p=0.10) | 0.064 (p=0.15) | 0.072 (p=0.11) |

The two municipality socioeconomic variables were then considered in the analyses. For each of them, we observed a graded increase in CHD incidence with decreasing socioeconomic position of the municipality of residence (Table 4, descriptive data). A perhaps stronger gradient was observed for the municipality percentage of CEOs than for the percentage of inhabitants with a university degree.

Table 4: Percentage of CHD incident cases in each quartile of municipality characteristics, GAZEL cohort, 1990-2000, men residing in high-urbanicity degree municipalities

|  | % of CHD events |
| --- | --- |
| Percentage of CEOs in the municipality | |
| 4th quartile | 1.70% |
| 3rd quartile | 1.86% |
| 2nd quartile | 2.52% |
| 1rst quartile | 2.92% |
| | Z= -2.70   p=0.003 * |
| | |
| Percentage of population with a university degree or equivalent | |
| 4th quartile | 1.86% |
| 3rd quartile | 1.93% |
| 2nd quartile | 2.56% |
| 1rst quartile | 2.64% |
| | Z= -1.84   p=0.032 * |

\* Cochran-Armitage trend test, bilateral

These two municipality variables were then introduced each into a separate multilevel model for CHD incidence adjusted for individual sociodemographic characteristics. As shown in Table 3 (third column), the municipality percentage of CEOs was significantly associated with CHD incidence after individual-level adjustment. In contrast, the association between municipality education and CHD incidence was no longer significant after controlling for individual sociodemographic characteristics (not shown in a table; hazard ratios for the third, second, and first quartiles of municipality education were 1.02 [95% CI: 0.61 to 1.70], 1.42 [95% CI: 0.88 to 2.30], and 1.34 [95% CI: 0.82 to 2.22]).

Original to the present article is the aim to assess how each of the CHD risk factors may contribute, independently, to the association between area socioeconomic position and CHD incidence. First, we estimated associations between each of the two area variables

considered separately and the different risk factors, adjusted for individual socioeconomic characteristics (Tables 5a and 5b). Overall, increased risks of overweight and obesity, smoking, and cholesterol were observed in low socioeconomic position municipalities (however, the municipality socioeconomic variables associated with the outcome was not the same for all risk factors).

All five risk factors were simultaneously introduced into the multilevel model for CHD. People with a higher BMI, smokers, and persons with hypertension and cholesterol had a higher risk of CHD incidence (Table 3). After controlling for risk factors, the CHD risk difference between municipalities with a low and high percentage of CEOs was not longer statistically significant, even if a pattern of association remained apparent.

In a final step, to assess the extent to which controlling for risk factors resulted in a decrease of the association between area socioeconomic position and CHD incidence, models for CHD incidence were reestimated with the percentage of CEOs introduced as an ordinal variable coded from 1 to 4. Such model was fitted to the data with either (i) no risk factors introduced into the model, (ii) each of the CHD risk factors included separately, or (iii) all risk factors considered simultaneously (results not shown). The association between the municipality percentage of CEOs and CHD incidence decreased by 13% when including all risk factors simultaneously into the model, suggesting that only a small part of the association was "explained" by risk factors. Inclusion of each risk factor into a separate model suggested that cholesterol (9% decrease) and smoking (6% decrease) made the largest contribution to this modest reduction in effect size.

Table 5a: Associations between municipality characteristics and body mass index (overweight and obesity) and smoking (former smoker and current smoker), from multilevel logistic models adjusted for individual socioeconomic characteristics, GAZEL cohort, 1990-2000, men residing in high-urbanicity degree municipalities

| | Overweight (vs. normal weight) | | Obesity (vs. normal weight) | | Former smoker (vs. non-smoker) | | Current smoker (vs. non-smoker) | |
|---|---|---|---|---|---|---|---|---|
| | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| **Percentage of CEOs in the municipality** | | | | | | | | |
| 4th quartile | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| 3rd quartile | 0.91 | (0.78 to 1.06) | 0.80 | (0.56 to 1.15) | 1.14 | (0.96 to 1.34) | 1.17 | (0.99 to 1.39) |
| 2nd quartile | 1.05 | (0.90 to 1.22) | 1.08 | (0.76 to 1.52) | 1.10 | (0.93 to 1.29) | 1.11 | (0.94 to 1.32) |
| 1rst quartile | 1.02 | (0.88 to 1.19) | 0.99 | (0.69 to 1.40) | 1.13 | (0.96 to 1.34) | 1.30 | (1.10 to 1.54) |
| Trend test | p=0.54 | | p=0.61 | | p=0.22 | | p=0.02 | |
| **Percentage of population with a university degree or equivalent** | | | | | | | | |
| 4th quartile | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| 3rd quartile | 0.96 | (0.83 to 1.12) | 1.23 | (0.85 to 1.80) | 1.11 | (0.94 to 1.31) | 1.04 | (0.88 to 1.23) |
| 2nd quartile | 1.26 | (1.08 to 1.47) | 1.43 | (0.98 to 2.01) | 0.99 | (0.83 to 1.17) | 0.94 | (0.79 to 1.12) |
| 1rst quartile | 1.28 | (1.10 to 1.50) | 1.61 | (1.11 to 2.35) | 1.21 | (1.01 to 1.44) | 1.04 | (0.95 to 1.35) |
| Trend test | p<0.001 | | p<0.01 | | p<0.11 | | p=0.54 | |

Table 5b: Associations between municipality characteristics and diabetes, hypertension, and cholesterol, from multilevel logistic models adjusted for individual socioeconomic characteristics, GAZEL cohort, 1990-2000, men residing in high-urbanicity degree municipalities

| | Diabetes | | Hypertension | | Cholesterol | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| **Percentage of CEOs in the municipality** | | | | | | |
| 4th quartile | 1.00 | | 1.00 | | 1.00 | |
| 3rd quartile | 1.69 | (0.94 to 3.05) | 1.02 | (0.82 to 1.27) | 1.08 | (0.88 to 1.31) |
| 2nd quartile | 1.21 | (0.65 to 2.28) | 1.13 | (0.91 to 1.40) | 1.16 | (0.95 to 1.40) |
| 1rst quartile | 1.31 | (0.71 to 2.44) | 1.00 | (0.80 to 1.25) | 1.20 | (0.99 to 1.46) |
| Trend test | p=0.74 | | p=0.86 | | p=0.10 | |
| **Percentage of population with a university degree or equivalent** | | | | | | |
| 4th quartile | 1.00 | | 1.00 | | 1.00 | |
| 3rd quartile | 1.00 | (0.56 to 1.78) | 1.03 | (0.83 to 1.29) | 1.19 | (0.98 to 1.45) |
| 2nd quartile | 0.73 | (0.39 to 1.37) | 1.21 | (0.97 to 1.51) | 1.18 | (0.97 to 1.44) |
| 1rst quartile | 1.17 | (0.66 to 2.07) | 1.05 | (0.83 to 1.32) | 1.23 | (1.00 to 1.51) |
| Trend test | p=0.76 | | p=0.34 | | p=0.23 | |

## Discussion

As in other previous studies conducted in the US or Europe,[2][11][14][16][33][34] the

present work reports an association between an area socioeconomic variable and CHD

incidence, beyond effects of individual characteristics. Moreover, it was found that traditional CHD risk factors, though strongly associated with CHD, only mediated a modest part of the association between area socioeconomic position and CHD incidence. Perhaps smoking and cholesterol had a larger mediating role than other risk factors.

However, there are limitations to the present study. First, residential areas were defined on a broader scale than in previous studies.[34] It is interesting to note that an area "effect" was observed even at this scale. Second, assessment of common chronic conditions based on self-reports is a potential source of misclassification. However, some studies have reported a high agreement between self-reports and medical records for diabetes and hypertension,[35] even if self-reported chronic diseases are likely to be affected by under-reporting because of the associated stigma or lack of knowledge or denial.[36] Despite this limitation, associations between these risk factors and CHD were observed in our data. A reason may be that the participants, as part of a large national company, are followed yearly by physicians of the company.[19]

Strengths of the present study include the careful follow-up of CHD events[18] and the rather long follow-up period (11 years), as well as the fact that, to the best of our knowledge, no previous multilevel study of the association between area social variables and CHD has been conducted in France.

We first assessed geographic variations in CHD incidence over the French territory. Of interest was the finding that only high-urbanicity residents contributed to between-region variations in CHD incidence. This finding is coherent with those of a previous study that reported a certain homogeneity in CHD incidence among non-urban residents.[37]

The percentage of CEOs in the municipality was used to characterize the socioeconomic environment. Our *a priori* assumption in using this indicator was that CEOs may have the opportunity to choose the most attractive residential environments; thus the area

15

percentage of CEOs may constitute an accurate proxy of desirable, high-social status, and advantaged areas. After adjustment for several individual socioeconomic characteristics, we found that CHD risk increased with decreasing area percentage of CEOs (it should be noted, however, that the other area variable considered based on residents' educational attainment was not associated with the outcome). Based on previous literature,[38] a stronger association may be expected if the association was estimated on a more local scale (e.g., at the neighbourhood level).

In the literature, it is generally hypothesized that associations between area socioeconomic variables and CHD are to some extent mediated by the traditional cardiovascular risk factors.[34][39] However, empirically, most studies that explicitly tested this association[11][14][33][40][41][42][43][44][45][46][47][48][49][50] observed that the area–CHD associations remained unchanged or only slightly decreased or increased after introduction of the risk factors. The present study is coherent with this literature as the area–CHD incidence association only decreased by slightly more than 10% when 5 of the traditional risk factors were introduced into the model.

Original to the present study was the attempt to assess whether some of the traditional risk factors may have a more important role than other in mediating the association between area socioeconomic position and CHD incidence. To the best of our knowledge, all studies that considered several risk factors as potential mediators included them simultaneously into the model, not allowing to separate the mediating role of the different factors. Our results suggest that smoking and cholesterol may have a greater contribution than other risk factors in the area–CHD association.

Future studies will have to assess whether this result is generalisable to other populations, and more importantly, to identify the other numerous processes involved in that

16

part of the association between area socioeconomic position and CHD that is not "explained" by traditional cardiovascular risk factors.

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**What this paper adds**

*What is already known on this subject?*

Several studies have suggested that cardiovascular risk factors may partly mediate the well-documented association between socioeconomic environmental variables and coronary heart disease (CHD). However, previous studies have assessed the *overall* mediating role of cardiovascular risk factors, but have never investigated the *specific* mediating role of each risk factor, not allowing disentangling their specific contribution to the area socioeconomic position–CHD association.

*What does this study add?*

After estimating socioeconomic environmental effects on CHD, we assessed the extent to which this contextual effect was mediated by each of the CHD risk factors. When risk factors were introduced into the model for CHD, we observed a modest decrease in the association

between area socioeconomic position and CHD. Risk factors that contributed most to the

association were smoking and cholesterol.