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Neighborhood deprivation and risk of head and neck cancer:

A multilevel analysis from France

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Abstract

Background While it is known that cancer risk is related to area-level socioeconomic status, the extent to which these inequalities are explained by contextual effects is poorly documented especially for head and neck cancer.

Methods A case-control study, ICARE, included 2415 head and neck cancer cases and 3555 controls recruited between 2001 and 2007 from 10 French regions retrieved from a general cancer registry. Individual socioeconomic status was assessed using marital status, highest educational level and occupational social class. Area-level socioeconomic status was assessed using the French version of the European Deprivation Index (EDI). The relationship between both individual and area-based socioeconomic level and the risk of head and neck cancer was assessed by multilevel analyses.

Results A higher risk for head and neck cancer was found in divorced compared with married individuals (OR=2.14, 95% CI=1.78–2.57), for individuals with a basic school-leaving qualification compared with those with higher education (OR=4.55 95% CI=3.72–5.57), for manual workers compared with managers (OR=4.91, 95% CI=3.92–6.15) and for individuals living in the most deprived areas compared with those living in the most affluent ones (OR=1.98, 95% CI=1.64–2.41). The influence of area-level socioeconomic status measured by EDI remained after controlling for individual socioeconomic characteristics (OR=1.51; 95% confidence interval: 1.23–1.85, p-value=0.0003).

Conclusions The role of individual socioeconomic status in the risk of head and neck cancer is undeniable, although contextual effects of deprived areas also increase the susceptibility of individuals developing the disease.

Keywords Upper aerodigestive tract cancer, socioeconomic status, neighborhood deprivation, multilevel analysis, case-control studies.

Introduction

Social inequalities in cancer incidence have been reported worldwide and for many cancer sites. An increased incidence in deprived populations has been observed for lung [1-4,] head and neck [1,3-5], liver[1,5], cervix[1,4-6], bladder [4], stomach [1,5] and esophagus [1,5,7] and an increased incidence in affluent populations has been observed for breast [1,4,5,8] and prostate cancer [1,4,5,9], and for melanoma, [1,4,5,10]. The influence of area-based socioeconomic level on the incidence of cancer is well documented in the literature but the underlying mechanisms that create these associations are rarely addressed.

It is currently unclear whether the higher incidence in disadvantaged areas is correlated with the higher proportion of disadvantaged individuals in these areas (composition effect) or if other aspects specific to the areas (positive or negative externalities) are associated with cancer risk (context effect). For example, regarding context effects, the social environment of the residence area is thought to have an influence on the percentage of smokers [11]. It has also been demonstrated that lower neighborhood socioeconomic status and higher convenience store concentration can be associated with a higher proportion of smokers after accounting for individual characteristics [12]. Others suggest that people living in the most deprived areas in some countries have greater exposure to environmental pollution [13]. More generally, the lives and health of individuals are affected not only by their personal characteristics but also by characteristics of the social groups (service availability, environmental exposition, job, education and leisure opportunities) to which they belong.

It appears essential to estimate the association between area-based socioeconomic level and incidence after controlling for individual socioeconomic variables to understand the extent of both composition effects and contextual effects. To our knowledge, while four studies of this type have focused on breast cancer [8,14-16], three on prostate cancer [15-17], three on colorectal cancer [16,18,19] and three on lung

cancer [16,17,20] none has investigated head and neck cancer despite being one of the sites most affected by social inequalities in cancer incidence [1].

The objective of this study was to explore the hypothesis that a contextual effect could explain part of the higher incidence of head and neck cancers in deprived areas. This was done by jointly evaluating the influence of individual and area-based socioeconomic level on the incidence of cancer by performing a multilevel analysis [21] of data from the case-control study ICARE.

Materials and methods

Study population

The ICARE study design has been previously published [22]. Briefly, it is a multicenter case-control study on lung and head and neck cancers in the general population conducted between 2001 and 2007 in 10 French regions retrieved from a general cancer registry. The registry comprises approximately 13% of the French population (7.6 million inhabitants). Only histologically confirmed cases aged ≤ 75 at the time of diagnosis identified between 2001 and 2007 and living in one of the 10 regions of the study were eligible. 2415 cases of head and neck cancer were included. Controls were selected by list-assisted random digit dialing sampling, in the same “départements” as the cases, using incidence density sampling method. Recruitment of controls was done by telephone by a polling institute experienced in this type of procedure. Controls were frequency-matched to the cases by sex, age (in 4 categories: less than 40, 40-54, 55-64, >65). Additional stratification was used to achieve a distribution by socioeconomic status among controls comparable to that of the general population. 3555 control individuals were interviewed. The distribution of the main occupational and economic activity characteristics of the active population of the regions in the study is similar to their distribution in France [22].

Individual socioeconomic variables

Specifically trained investigators interviewed the subjects. The questionnaire included a demographic section consisting of variables: age, marital status and educational attainment. It also included a history of occupied professions. Marital status (married, widower, single, divorced), educational attainment (Higher degree meaning college degree, A-level allowing for university entrance, technician level meaning the obtaining of a technical qualification, basic school meaning compulsory minimum level), and category of longest period of occupation (manager meaning an individual with management responsibility, farmer meaning person engaged in agriculture, mid-level manager between managers and employees, employee performing office tasks, artisan meaning a skilled manual worker in a particular craft, manual worker performing manual tasks) during one's lifetime were used to assess socioeconomic status at the individual level.

Area-based socioeconomic variables

The last known address of the cases and controls was geocoded and assigned to an IRIS (Ilots Regroupés pour l'Information Statistique), the smallest French area for which census data are available. Deprivation level of each IRIS was assessed using the EDI (European Deprivation Index) calculated from the 2007 census [23]. The methodology used an individual deprivation indicator from the conceptual definition of deprivation and selected ecological census variables that are the most closely related to the individual deprivation indicator in the European Union Statistics on Income and Living Conditions tool. This was available as a continuous variable, increasing from -17.35 to 51.12. A categorical version of the EDI (quintiles calculated at the French level) was used. Owing to poor health, some subjects (257 cases and 74 controls) were interviewed using a shorter version of the questionnaire that did not include the residential history. In addition, because the geocoding process required the exact address of the individual to assign geographic coordinates in space (latitude, longitude) and then assign an IRIS, 227 cases and 282 controls

were excluded because their address was incomplete. The final database included 1931 head and neck cancer cases and 3199 controls (Table 1). The subjects in the study were distributed in 2918 IRIS.

Statistical analysis

To study the relationship between socioeconomic level and risk of head and neck cancer, we used multilevel analyses justified by the non-independence of observations of subjects from the same geographical unit. This was done because of the hierarchical structure of individual data (level 1) and socioeconomic area-based data (level 2) [24].

- Step 0: Detection of potential existence of a 'group' effect

The first step of the multilevel analysis is based on analyzing the empty model without any explanatory variable. It contains only the random effects at the IRIS level and can detect the potential existence of a 'group' effect, which is also known to be the context effect on the dependent variable, i.e., the risk.

To verify the existence of a context effect, it is necessary to test the null hypothesis that the variance called level 2 variance (V_2) is null. V_2 quantifies the change in risk of one IRIS to another depending on the characteristics of IRIS. If this hypothesis is rejected, the multilevel model is justified.

- Step 1: Introduction of individual explanatory variables (model 1).

The second step is to add to model 0 the individual variables (marital status, educational attainment, occupational classification) related to the dependent variable in univariate analyses with a 5% threshold.

We tested whether variations between IRISs were still persistent after adding individual-level variables and observed if the V_2 declined with the addition of these variables. If it was the case, this would indicate that certain characteristics of the IRIS (context effect) were associated with the likelihood of having cancer.

The addition of these individual variables can also identify a possible composition effect. A composition effect exists if the V_2 decreases, indicating that some of the variations between the IRISs are due to differences in composition in terms of individual characteristics.

- Step 2: Introduction of the area-based explanatory variable (model 2).

The area-based variable EDI is added to model 1 if it is related to the risk of developing a cancer with a 5% threshold.

The analyses were performed using SAS version 9.3.

Results

Table 1 summarizes the individual and collective characteristics of individuals. The first four columns show the distribution of cases and controls according to the individual and area-based variables. The 5th and 6th columns present the results of the univariate regression models of status case/control of each variable independently while adjusting for sex, age and for the IRIS random intercept to examine each association.

Single or divorced individuals were more likely to develop head and neck cancer than married individuals with A-level, a technician level or a basic school-leaving qualification were more likely to have head and neck cancer than those with higher education. Individuals who were middle managers, employees, artisans and manual workers were a higher risk of developing head and neck cancer than managers (Table 1). Regarding the area-based socioeconomic variable, residing in a more deprived IRIS was associated with a higher risk of head and neck cancer, the highest risk being that of the most disadvantaged group compared with the most affluent one (OR=1.98, 95% CI=1.64–2.41).

In model 0 (Table 2), the change in risk between IRISs ($V_2=0.19$) was relatively low, but the variation was observed ($p=0.0022$), which justified the use of multilevel models. In model 1, V_2 declined by 14.94% after

the addition of individual variables to model 0. The differences between IRISs were lower when adjusted for individual variables, which highlighted the presence of a composition effect. Risk disparities between IRISs were explained at least partly by individual socioeconomic factors.

In model 2 with individual and area-based variables (model 2), the influence of area-level socioeconomic status as measured by EDI remained after controlling for individual socioeconomic status (OR=1.51; 95% confidence interval: 1.23–1.85, p-value=0.0003). This highlighted the persistence of the context effect after adjusting for individual variables. Adding the deprivation index reduced the variance between IRISs by 19.92% (from 0.1914 to 0.1596) compared with model 0 and by 2.01% (from 0.1628 to 0.1596) compared with model 1. Among the social disparities of risk, 95% were explained by a composition effect and 5% by a context effect i.e. by the characteristics of the IRIS, after taking into account the fact that disadvantaged people tend to live in the same places.

The test for cross-level interactions between the individual socioeconomic variables and area-based deprivation score on head and neck cancer risk showed no meaningful interactions.

Discussion

Individual-level deprivation measured using marital status, educational level, and occupational social class was associated with a higher risk of head and neck cancer. Area-level socioeconomic status as measured by the EDI was also associated with a higher risk of head and neck cancer. An important part of the association between area-level deprivation and head and neck cancer risk is compositional, meaning that people living in lower socioeconomic areas are themselves of lower socioeconomic status and are at increased risk of disease regardless of where they live. However, the association between area deprivation and cancer risk remained after controlling for individual socioeconomic status, meaning that the risk of head and neck cancer was potentially influenced by contextual factors.

Previous studies have examined the simultaneous impact of socioeconomic level measured at both the individual and area-based level, but none has examined the relationship with the incidence of head and neck cancer. Therefore, our results cannot be compared with those in the literature. Previous studies addressed prostate, breast, colon-rectum, and lung cancer, and most of them concluded that contextual factors had an effect after adjusting for individual socioeconomic level.

A study conducted by Meijer *et al.* [15] in Denmark between 2004 and 2008 reported that area characteristics were of greater importance in the incidence of lung cancer. Another study conducted by Li *et al.* [20] in Sweden between 2000 and 2010 found that neighborhood-level deprivation remained associated with lung cancer incidence after adjusting for individual-level sociodemographic variables and comorbidities.

Hastert *et al.* [16] in the United States between 2000 and 2002 observed that after controlling for demographics and for individual educational level and household income, the association between area-level socioeconomic status and prostate and breast cancer incidence didn't exist. Living in areas with the lowest socioeconomic status was associated with higher lung and colorectal cancer incidence. These results suggest that there are moderate-to-large associations between area-level socioeconomic status and specific cancer outcomes that are not completely explained by individual socioeconomic status.

A study conducted by Sanderson *et al.* [17] between 2000 and 2002 in the United States that focused on prostate cancer risk found that after adjusting for race, age, geographic region, and prostate-specific antigen testing, men with a college degree were at reduced risk for prostate cancer, as were men in the highest quartile of area-level socioeconomic status. The independent negative associations persisted when assessing individual-level and area-level socioeconomic status simultaneously.

Webster *et al.* [14] studied this hypothesis on breast cancer. The results for models including both measures were consistent with a contextual effect of socioeconomic status on the risk of breast cancer.

regardless of individual socioeconomic status. Another conducted by Robert *et al.* [8] found that after controlling for individual education and other individual risk factors, women were at elevated risk for breast cancer if they lived in the highest socioeconomic communities compared with those living in the lowest socioeconomic communities.

Finally, two studies focused on colorectal cancer. The first one conducted by Doubeni *et al.* [18] found that socioeconomic status, assessed by either individual-level education or neighborhood measures in a multilevel model, was associated with the risk of colorectal cancer even after controlling for other risk factors. Another one conducted by Kim *et al.* [19] focused more on behavioral pathways and found that living in a higher-SES neighborhood may protect against colorectal cancer in higher-educated women, and that the association was mediated by selected behavioral risk factors.

These results show consistency with our findings despite focusing on different cancer sites. There are no established standards for measuring area-based social level, making it difficult to directly compare results between studies. Even though the role of individual socioeconomic status in cancer incidence has been previously demonstrated, and is confirmed in the present study, the potential involvement of the characteristics of deprived areas cannot be excluded.

It has been hypothesized that residents of deprived neighborhoods have poorer access to high-quality food environments and to sports facilities, and have greater access to tobacco and alcohol outlets [25]. A study conducted by Black *et al.* [26], confirmed the finding that neighborhoods vary in terms of factors that could be expected to influence diet and exercise, including the price and availability of healthy food, and the number, proximity, and types of food stores available. Another study found that tobacco outlets were more densely located in areas of higher socioeconomic deprivation [27]. The same could apply to alcohol because another study found that the most deprived neighborhoods had substantially higher levels of alcohol outlet density than the least deprived ones (45.5% vs 14.8%, respectively) [28]. However, these

studies were conducted in the United States and in New Zealand where the social context is probably different from that in France, and where unfortunately no such study has been carried out.

Other possible mechanisms potentially link deprived areas to cancer risk. One possible pathway could be the psychological stress induced by certain characteristics of deprived areas, including higher population density, vandalism, criminality, excessive noise, economic, education and occupational opportunities. Stress is a condition of the mind-body interaction and a factor in the expression of disease that differs among individuals. It is not just dramatic stressful events are burdensome, but rather the many events of daily life that elevate and sustain the activities of physiological systems and cause sleep deprivation, overeating and other health-damaging behaviors. These all culminate toward feeling “stressed out”. Over time, this results in wear and tear on the body, called “allostatic load”, and it reflects not only the impact of life experiences but also genetic load, individual lifestyle habits reflecting items such as diet, exercise, substance abuse, alcohol and smoking and developmental experiences that set life-long patterns of behaviors and physiological reactivity. In the long run, allostatic load causes changes in the body that can lead to disease [29]. Until now, this hypothesis has only been demonstrated in cardiovascular diseases [30].

Our study has some limitations. Despite adjusting for the multilevel model with multiple individual socioeconomic variables such as marital situation, higher educational level, and occupation, the remaining association could be at least partly due to other socioeconomic variables like income and wealth, which was not recorded in the questionnaire. The ICARE study is a multicenter case-control study in the general population ensuring representativeness and good quality data. However, the number of subjects per IRIS is low, which reduces the statistical power of the analysis. The subjects of the study were interviewed by specifically trained investigators, but we cannot exclude a potential response bias in the data. A selection bias cannot be excluded either in this type of study. Finally, the area-based socioeconomic variable was

measured at the inclusion of the subjects, using their current address but ignoring their history of geographical mobility, which could be between two IRISs with different deprivation indices. Misclassification of the EDI quintile could occur if subjects were placed in the wrong IRIS with a different quintile than the recorded IRIS.

The strengths of the study include diagnostic confirmation obtained from general cancer registries. Because diagnosis and individual data collection for the registries was done by specifically trained investigators and not by questionnaires sent by mail, response bias and selection bias were reduced, thus ensuring good reliability. This allowed us to include three measures of individual-level socioeconomic status.

To our knowledge, this is the first study to explore the hypothesis of a contextual effect explaining part of the higher incidence of head and neck cancers in deprived areas. The role of individual socioeconomic status mediated by health-damaging behaviors is undeniable but the contextual effects of deprived areas also increase the susceptibility of individuals to develop the disease. In addition to measures focused on the behaviors of deprived individuals, health care policies should also consider improving their living environment.

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Table 1: Individual and aggregate characteristic of study population and their association with UADT cancer

| | Case (n=1931) | | Control (n=3199) | | | |
|-----------------------------|------------------|------------|---------------------|------------|--------------------------|---------|
| | Number | Percentage | Number | Percentage | OR ^a (CI 95%) | p-value |
| Individual variables | | | | | | |
| Marital status | | | | | | <0.0001 |
| Married | 1293 | 67.03 | 2448 | 76.60 | 1 | |
| Widower | 101 | 5.24 | 219 | 6.85 | 1.07 (0.82–1.40) | |
| Single | 215 | 11.15 | 237 | 7.42 | 1.75 (1.42– 2.16) | |
| Divorced | 320 | 16.59 | 292 | 9.14 | 2.14 (1.78–2.57) | |
| Educational attainment | | | | | | <0.0001 |
| Higher degree | 211 | 11.13 | 828 | 26.23 | 1 | |
| A-level | 147 | 7.76 | 366 | 11.59 | 1.67 (1.30–2.16) | |
| Technician level | 876 | 46.23 | 1267 | 40.13 | 2.84 (2.37–3.41) | |
| Basic school | 661 | 34.88 | 696 | 22.05 | 4.55 (3.72–5.57) | |
| Occupational classification | | | | | | <0.0001 |
| Manager | 119 | 6.25 | 552 | 17.33 | 1 | |
| Farmer | 52 | 2.73 | 189 | 5.93 | 1.28 (0.88–1.87) | |
| Mid-level manager | 206 | 10.82 | 634 | 19.90 | 1.53 (1.18–1.99) | |
| Employee | 310 | 16.28 | 601 | 18.86 | 2.87 (2.22–3.73) | |
| Artisan | 124 | 6.51 | 157 | 4.93 | 3.83 (2.78–5.28) | |
| Manual worker | 1093 | 57.41 | 1053 | 33.05 | 4.91 (3.92–6.15) | |
| Area-based variable | | | | | | |
| EDI quintile | | | | | | <0.0001 |
| 1 (most affluent)marital | 334 | 17.39 | 726 | 22.82 | 1 | |
| 2 | 403 | 20.98 | 660 | 20.75 | 1.14 (0.93–1.38) | |
| 3 | 375 | 19.52 | 585 | 18.39 | 1.45 (1.19–1.76) | |
| 4 | 329 | 17.13 | 645 | 20.28 | 1.44 (1.19–1.75) | |
| 5 (most deprived) | 480 | 24.99 | 565 | 17.76 | 1.98 (1.64–2.41) | |

^a Univariate analyses adjusted for age and sex, OR=Odd ratio

Table 2: Influence of socioeconomic level on risk of UADT cancer, multilevel analysis

| | Model 0 | Model 1 | | Model 2 | | | |
|-----------------------------|---------|-----------------|---------------------|---------|--------|---------------------|---------|
| | | OR ^a | CI ^b 95% | p-value | ORa | CI ^b 95% | p-value |
| Individual variables | | | | | | | |
| Age; mean | | 0.99 | 0.99-1.00 | 0.1119 | 0.994 | 0.987–1.001 | 0.0850 |
| Sex | | | | <0.0001 | | | <0.0001 |
| Man | | 1 | | | 1 | | |
| Woman | | 0.64 | 0.53-0.78 | | 0.636 | 0.527–0.768 | |
| Marital status | | | | <0.0001 | | | <0.0001 |
| Married | | 1 | | | 1 | | |
| Widower | | 0.89 | 0.67-1.18 | | 0.859 | 0.649–1.137 | |
| Single | | 1.61 | 1.29-2.00 | | 1.579 | 1.265–1.973 | |
| Divorced | | 1.96 | 1.62-2.37 | | 1.905 | 1.571–2.311 | |
| Educational attainment | | | | <0.0001 | | | <0.0001 |
| Higher degree | | 1 | | | 1 | | |
| A-level | | 1.33 | 1.02-1.74 | | 2.311 | 0.964–1.651 | |
| Technician level | | 1.64 | 1.32-2.03 | | 1.590 | 1.280–1.975 | |
| Basic school | | 2.36 | 1.86-3.01 | | 2.245 | 1.761–2.862 | |
| Occupational classification | | | | <0.0001 | | | <0.0001 |
| Manager | | 1 | | | 1 | | |
| Farmer | | 0.81 | 0.54-1.21 | | 0.800 | 0.530–1.207 | |
| Mid-level manager | | 1.31 | 0.10-1.72 | | 1.339 | 1.021–1.757 | |
| Employee | | 2.00 | 1.50-2.66 | | 1.965 | 1.475–2.618 | |
| Artisan | | 2.74 | 1.94-3.86 | | 2.724 | 1.930–3.843 | |
| Manual worker | | 3.06 | 2.34-3.99 | | 3.041 | 2.328–3.973 | |
| Area-based variable | | | | | | | |
| EDI quintile | | | | | | | 0.0003 |
| 1 (most affluent) | | | | | 1 | | |
| 2 | | | | | 1.049 | 0.852–1.292 | |
| 3 | | | | | 1.316 | 1.070–1.619 | |
| 4 | | | | | 1.281 | 1.044–1.571 | |
| 5 (most deprived) | | | | | 1.509 | 1.231–1.850 | |
| V2 | 0.1914 | 0.1628 | | | 0.1596 | | |
| Standard Error | 0.0671 | 0.0740 | | | 0.0745 | | |

^a Odd ratio; ^b Confidence Interval