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Neighborhood deprivation and prostate cancer mortality: a multilevel analysis from Sweden

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ABSTRACT

The objective was to analyze the association between neighborhood deprivation and prostate cancer mortality, after adjusting for individual characteristics. This study was designed as a follow-up study of prostate cancer mortality between 1 January 1990 and 31 December 2008 in patients aged 25-74 years (a total of 73,159 patients). Multilevel logistic regression analyses were performed with individual-level characteristics at the first level and level of neighborhood deprivation at the second level. The age-standardized prostate cancer mortality rate was 1.5 times higher in men living in high-deprivation neighborhoods than in those living in the most affluent neighborhoods. Mortality rates were also associated with certain individual-level characteristics, i.e. age, marital status, family income, educational attainment, immigration status, urban/rural status, mobility, and comorbidity. For example, there was a strong relationship between prostate cancer mortality and being unmarried, having a low income or educational attainment, and hospitalization for chronic obstructive pulmonary disease. In the full model, the risk of prostate cancer mortality was 25% higher in men living in the most deprived neighborhoods than in those living in the most affluent neighborhoods. High level of neighborhood deprivation independently predicts prostate cancer mortality. This raises important clinical and public health concerns. Both individual- and neighborhood-level approaches are important in healthcare policies.

INTRODUCTION

Prostate cancer is the most common male-specific cancer in developed countries. However, its predictors are not fully examined. In addition to age, androgen levels, and family history, studies have consistently shown associations between individual-level socioeconomic status (SES) and prostate cancer risk and survival [1-8]. For example, a study from Switzerland showed that patients with low occupational status had a 2-fold increased risk of dying from prostate cancer because of delayed diagnosis, poor examinations, and less invasive treatments [9].

During the first decade of this millennium an increasing number of studies have described the separate influences of individual- and neighborhood-level SES on health [10-14]. However, only a few studies have documented the effects of neighborhood-level SES on prostate cancer risk [15-17]. To the best of our knowledge, no study to date has simultaneously analyzed the effect of neighborhood-level SES on prostate cancer mortality, after adjusting for individual-level characteristics.

This multilevel study analyzes death from prostate cancer in all Swedish men aged 25-74 years living in 7,187 neighborhoods (of whom 73,159 were diagnosed with prostate cancer). The first aim of this study is to analyze whether there is an association between neighborhood deprivation and prostate cancer mortality. The second aim is to analyze whether this association remains after accounting for individual-level characteristics.

MATERIAL AND METHODS

Data Sources: the MigMed 2 Database

Data used in this study were retrieved from the MigMed 2 Database, maintained at the Center for Primary Health Care Research at Lund University, Sweden. MigMed 2 was constructed by linking data from several national Swedish data registers, including, but not limited to, the Total

Population Register, the Multi-Generation Register, the Migrant Register, and the Swedish Cancer Registry (1958-2008). Information from the various registers in the database is linked at the individual level via the national 10-digit civic registration number assigned to each person in Sweden for his or her lifetime. Prior to the inclusion of this information in the MigMed 2 Database, civic registration numbers were replaced with serial numbers to preserve anonymity. The unique serial number was used to follow each individual in the national registers until death, emigration or end of the study. Thus, there was no "loss" to follow-up.

Study Population and Study Period

The study population was the male population of Sweden aged 25 to 74 years, and the study period was 1 January 1990 to 31 December 2008. We chose 1990 as the first year of the study period because this is the first year for which we have information on geocoded addresses. This information was needed to construct the neighborhood-level variable.

Outcome Variables

The outcome variable was mortality from prostate cancer. We used the Swedish Cancer Registry to identify primary diagnoses of prostate cancer in the study population during the study period. We then linked this information with records in the Cause of Death Register to identify deaths among prostate cancer patients during the same period. All cases of cancer in Sweden must be registered in the Swedish Cancer Registry. The completeness of cancer registration is currently considered to be close to 100%. Only primary neoplasms of the prostate classified according to the 7th revision of the International Classification of Diseases (ICD-7) (The Swedish Cancer Registry has transferred all the cancer ICD codes into ICD-7) (code 177) were studied.

Neighborhood Deprivation Index: A summary measure was used to characterize neighborhood-level deprivation. We identified deprivation indicators used by past studies to characterize neighborhood environments and then used a principal components analysis to select deprivation

indicators in the Swedish national database. The following four variables were selected for those aged 25-74: low educational status (<10 years of formal education); low income (income from all sources, including that from interest and dividends, defined as less than 50% of individual median income);[18] unemployment (not employed, excluding full-time students, those completing compulsory military service, and early retirees); and social welfare assistance. Each of the four variables loaded on the first principal component with similar loadings (+.47 to +.53) and explained 52% of the variation between these variables.

A z score was calculated for each SAMS neighborhood. The z scores, weighted by the coefficients for the eigenvectors, were then summed to create the index.[19] The index was categorized into three groups: below one standard deviation (SD) from the mean (low deprivation), above one SD from the mean (high deprivation), and within one SD of the mean (moderate deprivation). Higher scores reflect more deprived neighborhoods.
The neighborhood-level variable was assessed in the year of the prostate cancer diagnosis for each patient.

Individual-Level Variables

Age Age ranged from 25 to 74 years and was divided into 10-year categories.

Marital Status Individuals were classified as married/cohabitating or single.

Family Income Information on family income in 1990 was obtained from the Total Population Register, which was provided by Statistics Sweden. We used this information to determine the distribution of family incomes in Sweden, and then used the distribution to calculate empirical quartiles.

Educational Attainment Educational attainment was classified as completion of compulsory schooling or less (≤ 9 years), practical high school education or some theoretical high school education (10–11 years), or theoretical high school and/or college education (≥ 12 years).

Immigrant Status Information was available on which country the men were born in. These countries were categorized as "Sweden" and "Others".

Urban/rural status was classified as living in a (1) large city, (2) middle-sized town, or (3) small town or rural area. The variable was included to allow adjustment for possible urban/rural differences in cancer treatment, access to screening, and lifestyle that might affect mortality.

Mobility: was classified as having "not moved" or "moved" to another neighbourhood with the same or a different level of deprivation in 5 years. Mobility was included in the model to minimise misclassification of the neighbourhood exposure

Comorbidities: *Chronic obstructive pulmonary disease (COPD)*: Patients' previous hospitalization for COPD, which was suspected to be one important prognostic factor for prostate cancer (as a surrogate for smoking), was identified in the Hospital Registry accordingly (ICD-10= J40-J49).

Statistical Analysis

Age-standardized incidence proportions were calculated by direct age standardization using 10-year age groups specific to men. Multilevel (hierarchical) logistic regression models with incidence proportions (the proportion of men who became cases among those who entered the study time interval) were used as the outcome variables. The analyses were performed using MLwiN, version 2.22. We created three models. Model 1 was the empty or unconditional model; model 2 included the neighborhood-level variable (neighborhood deprivation); and model 3 included the neighborhood-level variable and the individual-level variables: age, marital status,

immigration status, urban/rural status, family income, educational attainment, mobility, and comorbidity.

All statistical tests were two-sided. **Fixed Effects** The fixed effects are presented as odds ratios (ORs). We used multilevel logistic regression [20, 21] to estimate ORs with 95% confidence intervals (CIs) and P-values. Logistic regression provides a good approximation of Cox's proportional hazards model when the sample size is large, the outcome incidence rate is low, the follow-up time is relatively short, and the risk ratios are of moderate size.

Random Effects The between-neighborhood variance was estimated both with and without a random intercept and was considered significant if more than 1.96 times the size of the standard error, in accordance with the precedent set in previous studies [13, 22].

For comparison, we also calculated Cox regression models and logistic regression models using the SAS statistical package (version 9.2; SAS Institute, Cary, NC, USA).

Ethical Considerations

The study was approved by the Lund University Ethics Committee.

RESULTS

A total of 73,159 men were diagnosed with prostate cancer between 1990 and 2008 (Table 1), of whom 21,226 (29.0%) died during the study period; 10,153 died due to prostate cancer. More than two thirds of the patients were married and 93.6% were born in Sweden. The age-standardized mortality rate increased with increasing level of neighborhood deprivation. The overall mortality rate was 247.1 per 1,000 cases in low-deprivation neighborhoods, increasing to 288.5 per 1,000 cases and 356.1 per 1,000 cases in moderate- and high-deprivation

neighborhoods, respectively. Mortality rates were also higher in men with certain individual-level characteristics (age, marital status, family income, education, immigration status, urban/rural status, mobility, and comorbidity).

Table 2 shows the three different models, created through stepwise inclusion of the neighborhood- and individual-level variables. The odds of all-cause mortality increased as the level of neighborhood deprivation increased. Men living in the most deprived neighborhoods exhibited a 25% higher risk of all-cause mortality (OR=1.25, 95% 1.17-1.34) than those living in the most affluent (neighborhoods, after adjusting for age, marital status, family income, educational attainment, immigration status, urban/rural status, mobility, and comorbidity (full model). Analysis of the effects of the individual-level variables on all-cause mortality showed that men who were older, were unmarried, had low family income or low-educational attainment, had moved, or been hospitalized for COPD had the highest odds of all-cause mortality.

The between-neighborhood variance (i.e. the random intercept) was more than twice the standard error in all models, indicating that there were statistically significant differences between neighborhoods in prostate cancer mortality after adjustment for the individual- and neighborhood-level variables. The proportion of the explained variance increased after stepwise inclusion of the neighborhood- and individual-levels variables, reaching 73% in the full model (Table 2). This implies that included neighborhood- and individual-level variables explained 73% of the total variance between neighborhoods.

Table 3 shows three different models for the risk of mortality due to prostate cancer. Men living in the poorest neighborhoods exhibited a 19% higher risk of prostate cancer-specific mortality (OR=1.19, 95% 1.10-1.29) than those living in the richest neighborhoods, after adjusting for the individual-level variables (full model).

Results from additional analyses (data not shown in tables)

For comparison, we also performed an analysis using Cox regression models; the hazard ratio for all cause mortality was 1.10 (95% CI=1.04-1.15) among men living in the poorest neighborhoods in the full model; for prostate cancer-specific mortality, the corresponding hazard ratio was 1.11 (95% CI = 1.04-1.19).

We performed an additional analysis using logistic regression models and the corresponding results were almost identical. The odds ratio of all-cause mortality was 1.26 (95% CI=1.18-1.34) for men living in the poorest neighborhoods in the full model, for prostate cancer-specific mortality, the corresponding odds ratio was 1.19 (95% CI = 1.10-1.29).

We also performed an additional analysis to test the effects of individual income within neighbourhoods. Men living in the poorest neighborhoods and with the lowest incomes had an odds ratio 1.84 (95% 1.64-2.06) of prostate cancer mortality (reference group was those living in the richest neighborhoods and with the highest incomes).

DISCUSSION

The main finding of this study is that neighborhood deprivation predicts the odds of mortality in men with prostate cancer. This association remained significant after adjustment for the individual-level variables. Based on the whole male population of Sweden aged 25-74 years, this study confirms that low socioeconomic status increases the risk of prostate cancer mortality [1-6, 23]. Therefore, both neighborhood- and individual-level perspectives are needed when studying socioeconomic factors and their relationships with prostate cancer mortality.

Various mechanisms have been proposed as possible explanations for neighborhood effects on individual health. In the present case, it is possible that living in deprived neighborhoods causes isolation from people with healthy behaviors that promote prostate cancer

survival, such as eating healthily, performing physical activity, and not smoking. All these factors may be mediators of the link between living in a deprived neighborhood and increased risk of prostate cancer mortality. However, in a multilevel study from the US, mortality risks remained higher in deprived neighborhoods even after adjustment for body mass index and smoking [24]. Multilevel studies from the US demonstrated the importance of income inequality for mortality [16, 17, 25]. In contrast, in Nova Scotia in Canada, a country with lower income inequality than the US, neighborhood socioeconomic characteristics were not significantly associated with mortality [26]. In the UK, previous studies have described neighborhood effects on health [27, 28] .

Living in deprived neighborhoods can cause isolation from health-promoting milieus (e.g., safe places to exercise and decent housing) and services. The experience of being discriminated against in deprived neighborhoods with a poor reputation may also contribute to a negative prostate cancer risk profile [25, 26, 29, 30]. In comparison with wealthy nations, associations between neighborhood characteristics and different health outcomes were inconsistent [31]. This implies that neighborhood determinants of health are complex. Such determinants may include access to healthcare, education, and social services. Access to these services is uneven in the US, where the effects of income inequalities on health are more pronounced [25]. For example, low income men are likely to present with later stage cancers [8].

Neighborhood-level inequities include unequal access to and quality of primary and secondary healthcare services [32] and may affect the relationship between prostate cancer screening and affordability of private health insurance [8, 33]. Opportunistic screening through prostate-specific antigen (PSA) testing became commonplace in the US at the end of the 1980s and in Sweden in the early 1990s. The frequency of prostate cancer diagnoses has increased substantially since the introduction of PSA screening. However, whether this screening is beneficial for prostate cancer survival is still uncertain [34].

In Sweden, medical care is provided to all permanent residents, and primary healthcare clinics and hospitals are equally distributed and located centrally in all types of neighborhoods [32]. However, the actual number of health professionals working in primary healthcare clinics can vary considerably by neighborhood type. This is due to difficulties in recruiting and retaining healthcare personnel in high-deprivation neighborhoods. The misdistribution of medical personnel across neighborhoods has also been documented in England, another country with universal health care [35].

Our study has some limitations. For example, we had no information regarding tumor stage at diagnosis, treatment, or other factors influencing prostate cancer survival. However, risk factors can be considered as mediators in the causal pathway between neighborhoods and prostate cancer mortality, rather than confounders. A second limitation is the fact that, in studies of neighborhood effects on health, selective residential mobility can cause compositional neighborhood differences. Selective residential mobility is the tendency of individuals to move to neighborhoods whose characteristics match their individual characteristics (for example, the tendency of individuals with low socioeconomic status to move to low-socioeconomic status neighborhoods). However, we adjusted for family income, which improved our possibilities to differentiate between compositional and contextual effects on prostate cancer mortality.

Our study also has several strengths. First, it was a population-based study covering all incident cases of prostate cancer in Sweden. The use of personal identification numbers made it possible to follow individuals in different registers, for example the Migrant Register, which permitted calculation of exact risk times. Second, the Swedish Total Population Register is highly complete, with very few missing data. For example, data for income were 99.4% complete. Finally, the use of multilevel modeling helped us to separate neighborhood-level and individual-level effects and allowed us to consider both fixed and random effects in the analyses.

CONCLUSIONS

Neighborhood deprivation has an independent contribution on mortality in men with prostate cancer. The individual-level and neighborhood-level variables cumulatively load against individuals so that the most at-risk men would be those who have both individual- and neighborhood-level risk factors. These findings raise important clinical and public health concerns, and indicates that both individual- and neighborhood-level approaches are important in health care policies.

CONFLICTS OF INTEREST

None

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Table 1. Distribution of population, number of prostate cancer events, and age-standardized mortality (per 1000) by neighborhood-level deprivation

	Population	Distribution (%)	All deaths	Deaths due to prostate cancer	Neighborhood deprivation		
					Low	Moderate	High
Total population (%)	73159				13757 (18.8%)	49254 (67.3%)	10148 (13.9%)
Death			21226	10153	247.1	288.5	356.1
Age (years)							
25-34	359	0.5	15	13	59.5	35.7	39.2
35-44	5948	8.1	313	231	33.9	51.8	92.6
45-54	20506	28.0	2163	1278	89.5	104.0	142.1
55-64	25994	35.5	6921	3624	230.8	263.5	324.2
65-74	20352	35.5	11814	5007	566.8	575.3	616.8
Marital status							
Married/cohabiting	52521	71.8	14123	6866	238.1	271.1	330.6
Never married, Widowed, or divorced	20638	28.2	7103	3287	284.1	333.3	399.2
Family income (quartiles)							
Low income	18368	25.1	7749	3572	279.2	317.1	381.0
Middle–low income	18244	24.9	6223	2864	249.4	304.2	368.0
Middle–high income	18258	25.0	4248	2124	250.0	276.3	335.2
High income	18289	25.0	3006	1593	227.3	242.2	289.5
Educational attainment							
Compulsory school or less (≤ 9 years)	23418	32.0	12329	5280	258.2	297.6	370.5
Practical high school or some theoretical high school (10–11 years)	11265	15.4	1790	982	113.2	118.0	150.3
Theoretical high school and/or college (≥ 12 years)	38476	52.6	7107	3891	110.1	128.7	161.3
Immigrant status							
Sweden	68442	93.6	20034	9599	246.5	288.4	358.8
Other countries	4717	6.4	1192	554	255.3	294.4	321.5
Urban/rural status							
Large cities	16326	22.3	4416	1875	237.7	282.3	358.0
Middle-sized towns	30580	41.8	8717	4237	247.9	289.0	346.9
Small towns/rural areas	26253	35.9	8093	4041	266.9	291.0	364.0
Mobility							
Not moved	64174	87.7	18889	9040	245.3	287.8	356.3
Moved	8985	12.3	2337	1113	261.3	291.5	356.8
Hospitalized for chronic lower respiratory diseases							
No	69662	95.2	19549	9742	243.1	283.7	346.9
Yes	3497	4.8	1677	411	325.0	377.2	477.8

Table 2. Odds ratios (OR) and 95% confidence intervals (CI) for all-cause mortality in men with prostate cancer; Results of multi-level logistic regression models

	Model 1			Model 2			Model 3			
	OR	95% CI		OR	95% CI		OR	95% CI		P-value
Neighborhood-level variable										
Low	1			1			1			
Moderate	1.19	1.13	1.25	1.11	1.06	1.17	1.02	0.97	1.07	0.484
High	1.64	1.54	1.74	1.46	1.37	1.56	1.25	1.17	1.34	<0.001
Age										
Age				1.14	1.14	1.14	1.12	1.12	1.13	<0.001
Marital status										
Married/co-habiting							1			
Never married, widowed, divorced							1.46	1.40	1.52	<0.001
Family income (quartiles)										
High income							1			
Middle-high income							1.23	1.17	1.31	<0.001
Middle-low income							1.35	1.28	1.43	<0.001
Low income							1.49	1.41	1.58	<0.001
Education attainment										
Compulsory school or less (≤ 9 years)							1.23	1.17	1.30	<0.001
Practical high school or some theoretical high school (10–11 years)							0.94	0.89	1.00	0.046
Theoretical high school and/or college (≥ 12 years)							1			
Immigrant status										
Sweden							1			
Others							0.98	0.90	1.05	0.549
Urban/rural status										
Large cities							1			
Middle-sized towns							1.02	0.97	1.08	0.368
Small towns/rural areas							1.04	0.99	1.10	0.194
Mobility										
Not moved							1			
Moved							1.15	1.09	1.22	<0.001
Hospitalized for chronic lower respiratory diseases										
No							1			
Yes							1.60	1.47	1.75	<0.001
Variance (S.E.)	*0.112 (0.009)*			*0.038 (0.008)*			*0.036 (0.008)*			
Explained variance (%)	*15*			*71*			*73*			

Table 3. Odds ratios (OR) and 95% confidence intervals (CI) for prostate cancer-specific mortality; Results of multi-level logistic regression models

	Model 1			Model 2			Model 3			
	OR	95% CI		OR	95% CI		OR	95% CI		P-value
Neighborhood-level variable										
Low	1			1			1			
Moderate	1.20	1.13	1.27	1.13	1.06	1.20	1.03	0.97	1.10	0.317
High	1.49	1.38	1.61	1.32	1.22	1.43	1.19	1.10	1.29	<0.001
Age										
Age				1.08	1.08	1.09	1.08	1.07	1.08	<0.001
Marital status										
Married/co-habiting							1			
Never married, widowed, divorced							1.24	1.18	1.30	<0.001
Family income (quartiles)										
High income							1			
Middle-high income							1.17	1.09	1.26	<0.001
Middle-low income							1.23	1.15	1.31	<0.001
Low income							1.35	1.26	1.45	<0.001
Education attainment										
Compulsory school or less (≤ 9 years)							0.98	0.92	1.04	0.549
Practical high school or some theoretical high school (10–11 years)							0.93	0.86	1.00	0.046
Theoretical high school and/or college (≥ 12 years)							1			
Immigrant status										
Sweden							1			
Others							0.97	0.88	1.07	0.549
Urban/rural status										
Large cities							1			
Middle-sized towns							1.19	1.12	1.27	<0.001
Small towns/rural areas							1.26	1.19	1.35	<0.001
Mobility										
Not moved							1			
Moved							1.07	1.00	1.15	0.036
Hospitalized for chronic lower respiratory diseases										
No							1			
Yes							0.62	0.54	0.70	<0.001
Variance (S.E.)	*0.098 (0.013)*			*0.059 (0.012)*			*0.052 (0.012)*			
Explained variance (%)	*13*			*47*			*54*			