

Sociodemographic Status, Stress, and Risk of Prostate Cancer. A Prospective Cohort Study

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PURPOSE: The social gradient in prostate cancer incidence observed in several studies may be a result of differential access to prostate cancer screening. We aim to assess if socioeconomic status, stress, and marital status are associated with prostate cancer risk in a population with free access to health care.

METHODS: The 5,496 men who participated in the Copenhagen City Heart Study were asked about their income, educational level, stress level, and marital status during 1981–1983. These men were prospectively followed up in the Danish Cancer Registry until the end of 2002 and fewer than 0.1 % were lost to follow-up.

RESULTS: During follow-up, 157 men were diagnosed with prostate cancer. Neither high income (HR = 1.17, 95% confidence interval [CI]: 0.78–1.76) nor high education (HR = 1.22; 95% CI: 0.76–1.96) were associated with risk of prostate cancer. There were also no differences in prostate cancer risk according to stress (HR = 0.99; 95% CI: 0.90–1.09) or marital status.

CONCLUSION: In a racially homogeneous population of Caucasians with free access to health care, we found no evidence of a relation between sociodemographic variables or stress and subsequent risk of prostate cancer.

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INTRODUCTION

Prostate cancer is among the most common malignancies in men, and it shows striking social disparities (1). Men of higher socioeconomic status (SES) seem to have an elevated incidence of prostate cancer compared to those of lower SES (2–4). For prostate cancer mortality, the picture is reversed with lower prostate cancer mortality rates among men with higher SES (4). These differences have mainly been ascribed to differential access to prostate-specific antigen (PSA) testing in different socioeconomic groups.

Socioeconomic disadvantage can lead to psychological stress. Animal models provide evidence that stress affects tumor growth and development (5), but few epidemiologic studies have assessed the relation between stress and risk of prostate cancer (6). In a large registry linkage study, no increased risk of prostate cancer was observed among men who

had experienced losing a child to cancer (6). The physiological reactions to acute stress from major life events such as losing a child or a spouse may be very different from those resulting from chronic “low-key” stress of everyday life. Repeated episodes of stress or chronic stress may weaken the immune system and render the individual susceptible to malignancies (5).

Marital status, as an indicator of social support, may be an important way of coping with socioeconomic disadvantages or stress and may thereby also affect prostate cancer risk. One study found that divorced and separated men had a higher risk of prostate cancer than married men (7). We aim to assess if the social disparity in prostate cancer incidence prevails in a racially homogeneous population of Caucasians with free access to medical care. We also aim to assess if perceived stress of everyday life and marital status are associated with risk of prostate cancer.

MATERIALS AND METHODS

Study Population

The Copenhagen City Heart Study is a longitudinal study initiated in 1976 (8). A random sample of men and women from Copenhagen were invited to participate in the study. A physical examination was performed and participants were asked to fill in a questionnaire regarding various risk factors.

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Selected Abbreviations and Acronyms

CI = confidence intervals
 HR = hazard ratio
 IGF-1 = insulin-like growth factor-1
 PSA = prostate-specific antigen
 SES = socioeconomic status

At the second examination during 1981–1983, the study participants were asked about their stress level; this information is used as baseline for the present study. The 12,698 participants (5,680 men) in the second examination constituted a response proportion of 70%. The vast majority of the participants were Caucasians and all participants gave informed consent. Men with prostate cancer before baseline ($n = 19$) and men who lacked information on stress ($n = 15$), educational level ($n = 12$), income ($n = 47$), marital status ($n = 5$), or other covariates ($n = 86$) were excluded, leaving 5,496 men for the analyses.

Sociodemographic Variables

All sociodemographic variables were based on self-reported information at baseline in the period 1981–1983. Educational level was reported in categories of low (<8 years), medium (8–11 years), and high (≥ 12 years) education. Income was divided into categories of low (<\$1,000 per month), medium (\$1,000–2,500 per month), and high

(>\$2,500 per month) income. Marital status categories were married, unmarried, divorced/separated, and widowed.

Perceived Stress

The study participants were asked about stress intensity and frequency in the period 1981–1983. In the questionnaire, stress was exemplified as the sensation of tension, nervousness, impatience, anxiety, or sleeplessness. *Stress intensity* was reported as (0) none, (1) light, (2) moderate, or (3) high. *Stress frequency* was reported as (0) never/hardly ever, (1) monthly, (2) weekly, or (3) daily. The two questions were added and combined into a 7-point stress score ranging from 0 (indicating no stress) to 6 (indicating high daily stress).

Covariates

Potential confounders were identified according to the causal diagram in Fig. 1. Age (continuous) was the main possible confounder of the associations of interest. The associations between the sociodemographic variables and risk of prostate cancer will therefore only be adjusted for age. SES and marital status were also possible confounders for the relation between stress and risk of prostate cancer. Physical activity, body mass index, and alcohol intake were either possible intermediates (as they are presented in the diagram) or potential confounders. The analysis of stress

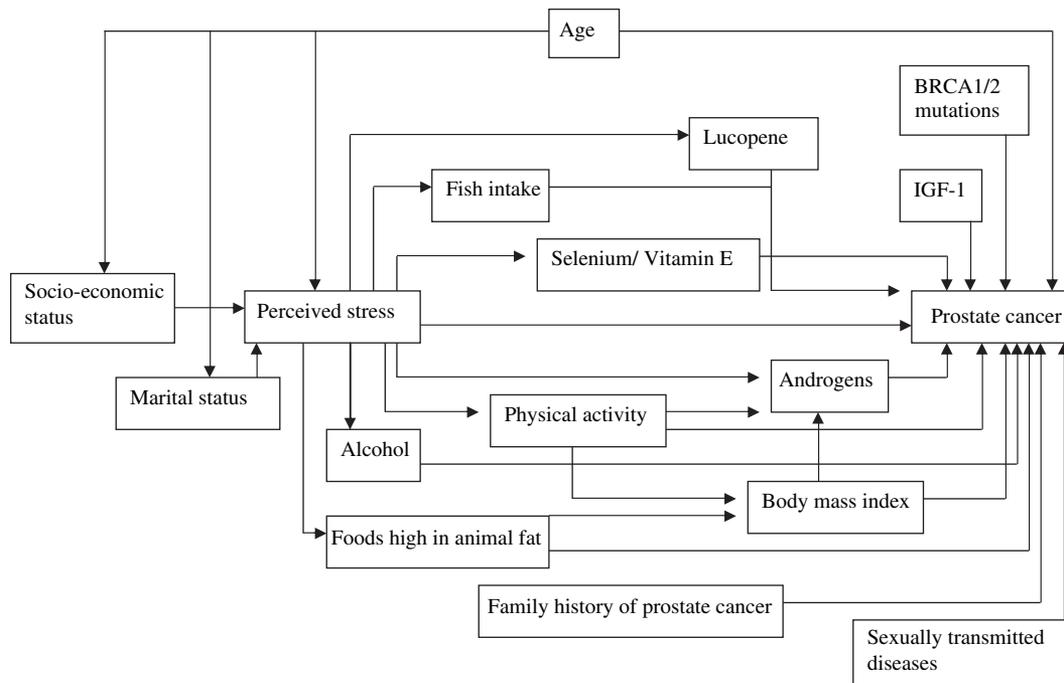


FIGURE 1. Causal diagram for the relation between socioeconomic status, marital status, perceived stress, and risk of prostate cancer. IGF-1 = insulin-like growth factor-1.

will therefore be presented both age-adjusted and with adjustment for age, sociodemographic factors, physical activity in leisure time (none or very little activity; 2–4 hours of light activity per week; >4 hours of light activity, or 2–4 hours of high level activity; and competition level or >4 hours of high level activity per week), body mass index (continuous), and alcohol intake (<1, 1–7, 8–14, 15–21, 22+ drinks/wk). Lycopene, fish intake, selenium/vitamin E, and foods high in animal fat are possible intermediates on the pathway from stress to prostate cancer, whereas insulin-like growth factor (IGF-1), *BRCA1/2* mutations, family history of prostate cancer, and sexually transmitted diseases were assumed not to be strongly associated with the sociodemographic factors or stress.

Follow-up

The participants were followed up from the date of the second examination until the date of first diagnosis of primary prostate cancer ($n = 157$), death ($n = 2889$), emigration out of Denmark ($n = 31$), or end of follow-up on December 31, 2002 ($n = 2419$). Using the civil registry number, which is unique to every Danish citizen, primary prostate cancer events were identified through linkage to the Danish National Cancer Registry. The following ICD-7 codes were used to identify primary invasive prostate cancer cases: 177.0, 477.0, and 877.0. The vital status of the participants was followed up in the Central Person Registry.

Statistical Methods

Data were analyzed by means of Cox proportional hazards models with age as the time variable. Initially, we estimated the age-adjusted hazard ratio (HR) of prostate cancer associated with the sociodemographic variables and stress. Second, a multivariate Cox proportional hazards model was fitted to adjust the association between stress and prostate cancer for potential confounding. Finally, PSA screening is less common in Denmark than in the United States and Canada, but introduction of PSA testing in the late 1980s may still have affected the diagnosis pattern in this population. We conducted separate analyses for follow-up periods before and after 1990 in order to address whether the introduction of PSA testing affected our estimates.

RESULTS

Sociodemographic Status, Stress, and Risk of Prostate Cancer

The mean age at baseline was 56 years ranging from 21 to 98 years. In the total study population, 45% had low education, 25% had low income, 22% were unmarried or divorced, and 6% reported high levels of stress. With an incidence rate of

TABLE 1. Risk of primary prostate cancer associated with sociodemographic variables and stress among 5,496 men participating in the Copenhagen City Heart Study in 1981–1983

	Cancers, n	Incidence per 100,000 yrs	Adjusted HR* (95% CI)
Income			
Low ($n = 1366$)	51	317	1 (reference)
Medium ($n = 2719$)	60	139	0.72 (0.49–1.05)
High ($n = 1411$)	46	193	1.17 (0.78–1.76)
<i>p</i> Value for trend			0.51
Education			
Low ($n = 2462$)	71	207	1 (reference)
Medium ($n = 2175$)	63	183	1.07 (0.76–1.50)
High ($n = 859$)	23	160	1.22 (0.76–1.96)
<i>p</i> Value for trend			0.42
Marital status			
Married ($n = 4035$)	122	197	1 (reference)
Unmarried ($n = 639$)	12	119	1.03 (0.57–1.86)
Divorced/separated ($n = 585$)	12	145	0.92 (0.51–1.67)
Widowed ($n = 237$)	11	419	1.09 (0.59–2.03)
Stress score (continuous)	157		0.99 (0.90–1.09)

CI = confidence interval; HR = hazard ratio.

*The associations between income, education, or marital status and prostate cancer are adjusted for age. The association between stress and prostate cancer is adjusted for age, income, educational level, marital status, alcohol intake, physical activity in leisure time, and body mass index.

317 per 100,000 years, men with low income had markedly higher incidence of prostate cancer than men with higher income (Table 1). This difference in risk could, however, mostly be explained by adjusting for age. Men with more than 12 years of formal education seemed to be at a slightly higher risk of prostate cancer (HR = 1.22; 95% CI: 0.76–1.96), but the estimates were unstable and there was no dose-response effect (*p* value for trend: 0.42). Widowed men had a markedly higher incidence of prostate cancer than any other marital group, but this could again be explained by age. The stress score was not associated with risk of prostate cancer (HR = 0.99; 95% CI: 0.90–1.09).

Influence from Period of Follow-up

During the 1980s, 41 men developed prostate cancer, while 116 men developed prostate cancer from 1990 and until the end of the study in 2002 (Table 2). Men with high income, with high education, or who were widowed all seemed to have a slightly higher incidence of prostate cancer in the first follow-up period. Stress seemed to be weakly associated with prostate cancer in an inverse manner in the first follow-up period (HR = 0.92; 95% CI: 0.75–1.14 per one unit increase in the 7-point stress score). However, the associations during this period were based on few cases and no clear trends were found. Prostate cancer incidence did not seem to be associated with stress or any of the sociodemographic variables in the last period of follow-up.

TABLE 2. Risk of primary prostate cancer associated with sociodemographic variables and stress according to period of follow-up

	Baseline-1989		1990-2002	
	Cancers, n	Multiadjusted HR* (95% CI)	Cancers, n	Adjusted HR* (95% CI)
Income				
Low	19	1 (reference)	32	1 (reference)
Medium	10	0.55 (0.25-1.23)	50	0.69 (0.43-1.09)
High	12	1.49 (0.70-3.18)	34	0.96 (0.58-1.59)
p Value for trend		0.46		0.98
Education				
Low	20	1 (reference)	51	1 (reference)
Medium	15	1.07 (0.55-2.08)	48	1.05 (0.71-1.55)
High	6	1.37 (0.55-3.41)	17	1.15 (0.66-1.99)
p Value for trend		0.55		0.63
Marital status				
Married	30	1 (reference)	92	1 (reference)
Unmarried	3	1.14 (0.35-3.73)	9	0.97 (0.49-1.92)
Divorced/separated	3	0.90 (0.27-2.96)	9	0.92 (0.46-1.82)
Widowed	5	1.36 (0.52-3.56)	6	1.07 (0.46-2.46)
Stress score (continuous)	41	0.92 (0.75-1.14)	116	1.00 (0.89-1.12)

CI = confidence interval; HR = hazard ratio.

*The associations between income, education, or marital status and prostate cancer are adjusted for age. The association between stress and prostate cancer is adjusted for age, income, educational level, marital status, alcohol intake, physical activity in leisure time, and body mass index.

DISCUSSION

In this racially homogeneous population with free access to health care, we found no evidence of social disparities in the incidence of prostate cancer, nor was the risk of prostate cancer associated with marital status or perceived stress. The fact that we found no social gradient in the incidence of prostate cancer is in contrast to the results from several large studies (3). A Finnish study found a higher incidence of prostate cancer among the higher social classes than the lower (9). A social gradient was also found in another registry-based study from the United Kingdom, in which aggregated data on socioeconomic factors were used to calculate a deprivation score (4). The authors found that men in the most affluent group had an incidence of prostate cancer that was approximately 50% higher than that of men in the most deprived group, whereas prostate cancer survival displayed a negative association with deprivation. In a study of 11,896 prostate cancer cases, Schwartz and colleagues (2) found that cases from the highest socioeconomic group were more likely to have local-stage disease than were those from the lowest socioeconomic group.

Access to PSA testing became widely available in most westernized countries in the late 1980s. SES may affect the access and utilization of the health care system including

PSA testing. Dutta and colleagues (4) found that the incidence trend between socio-economic groups primarily started to diverge after PSA testing became widely available. Health insurance is strongly associated with the use of prostate cancer screening. A plausible reason for the lack of a social gradient in the observed prostate cancer incidence in this study is that Denmark has a free health care system accessible to all Danes.

We found no association between stress and risk of prostate cancer despite the fact that prolonged stress may affect the immune (5) and hormonal (10) systems, both of which would be expected to alter the risk of prostate cancer. Although we used a very different measure of stress, our results are in agreement with the null result of a previous study on prostate cancer risk among men who had lost a child to cancer (6).

Strengths and Weaknesses

The prospective design of the Copenhagen City Heart Study ensured temporality between assessment of the exposures of interest and incidence of prostate cancer. Linkage of civil registry numbers to nationwide population-based registers enabled the identification of virtually all cases of diagnosed prostate cancer and allowed for nearly complete long-term follow-up.

Several previous studies have used ecological measures of SES derived from census registries (2,4). This is problematic if an individual is assigned to a socioeconomic group different from his actual socioeconomic position. We used individual measures to avoid this problem. We used self-reported measures of income and education as proxy measures of SES, and one may argue that these are only crude measures of a much more complex concept. However, we still expect that the measures of SES in this study were sufficient to reveal any major social disparities in prostate cancer incidence, since they are similar to the measures of SES that were used in a previous study that found a social gradient in prostate cancer incidence in Norway (7).

Stress was defined as an individual state of high arousal and displeasure (11). By using a measure of perceived stress, we accounted for the fact that each individual has different capacities and ways to cope with stressful situations (12). However, using two questions on stress intensity and frequency instead of using a more extensive scale may have resulted in some exposure misclassification, which could possibly partly explain why we found no association between stress and prostate cancer.

CONCLUSION

We found no evidence of a social gradient in the incidence of prostate cancer in a population with free access to medical care. Thus the social gradient observed in other studies

is most likely a result of differential usage of PSA testing. If early detection of prostate cancer indeed has an effect on prostate cancer-associated mortality, breaking down barriers for health care utilization and PSA screening may be a major public health issue in populations without free access to medical care. Also, prostate cancer risk did not seem to be associated with perceived stress or marital status.

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