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Differences according to socioeconomic status in the management and mortality in men with high risk prostate cancer

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ABSTRACT

Background: Outcomes for many cancer forms are associated with socioeconomic status (SES).We investigated if SES was associated with management and mortality in men with high risk prostate cancer.

Material and methods: A nation-wide population-based cohort in Prostate Cancer Data Base Sweden (PCBaSe), a merged database including data on incident prostate cancer identified in the National Prostate Cancer Register (NPCR) between 1997 and 2006. High risk PCa was defined as T3 tumour, and/or Gleason score 8–10 and/or PSA 20–50 ng/mL. Use of bone scan, curative treatment, and mortality in relation to SES was assessed by logistic, Cox, and competing risk regression with hazard ratios (HR), sub-distributed HR and 95% confidence intervals (CI) adjusted for co-morbidity, age, calendar period and clinical subgroups.

Results: Amongst 17,522 high risk prostate cancer patients, a bone scan was more often performed in higher white-collar than in blue-collar workers (OR 1.30; 95% CI 1.21–1.40). Amongst men without metastases, the likelihood of intention to treat was higher in higher white-collar workers (OR 1.43; 95% CI 1.28–1.57). In men who received curative treatment, the likelihood was higher to undergo radical prostatectomy for higher white-collar patients (OR 1.29; 95% CI 1.10–1.47). In men without metastases, not only overall mortality was lower amongst higher white-collar workers (HR, 0.76; 95% CI 0.60–0.97), but also prostate cancer-specific mortality (sHR 0.70; 95% CI, 0.49–0.99).

Conclusions: We conclude that socioeconomic disparities in the management and mortality in men with high risk prostate cancer exist also within the setting of a National Health Care System aiming to provide care on equal terms to all residents.

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1. Introduction

Cancer patients with low socioeconomic status (SES) in general have a poorer survival than those with high SES.[1] In recent studies, we have found evidence of social variations in the management and survival in patients diagnosed with lung-, colorectal- and breast-cancer in Sweden.[2–4] Over the past two decades, the incidence of prostate cancer (PCa), has increased rapidly in most Western countries,[5] with reports of a higher incidence in high compared to low SES groups.[6] In addition to studies describing poorer outcomes in low socioeconomic patients,[7–10] investigators have also found evidence of more advanced disease at date of diagnosis in men with PCa belonging to low socioeconomic groups.[11] Factors contributing to social variations in mortality may depend not only on tumour and host related factors, but also on factors related to unequal access and provision of health care. A recent study demonstrated clear socioeconomic variations in the likelihood to undergo radical prostatectomy or receive radiotherapy amongst PCa patients managed within the British National Health Care System.[12] For PCa patients with high risk disease, guidelines, including those in Sweden, recommend a metastatic work-up.[13,14] If no metastases are found amongst patients with high risk PCa, curative treatment is indicated if remaining life expectancy is estimated to exceed 5 years.[15] The aim of the present study was to examine possible associations between socioeconomic status, metastatic work-up, treatment and mortality in patients with high risk PCa managed in Sweden, a country with a tax-funded National Health Care System aiming to provide care to all residents on equal terms.

2. Material and methods

2.1. Data collection

The Prostate Cancer Data Base Sweden (PCBaSe) is a database of incident PCa cases recorded in the National Prostate Cancer Register (NPCR) of Sweden. Additional information has been retrieved from the Swedish Cancer Register (SCR), the National Patient Register (NPR), a Census database and the Cause of Death Register (CDR) through record-linkage using the Swedish personal identity number assigned to all residents in Sweden.[16] The NPCR of Sweden captures 98% of all PCa cases in Sweden since 1998.[17] Through December 31, 2006, this register contains data on more than 75,000 cases with information on mode of detection, TNM-stage, Gleason score (GS), serum levels of prostate specific antigen (PSA) and primary treatment within 6 months of date of diagnosis. The NPR includes information on hospital admissions and discharges from all public hospitals and each inpatient record contains date of hospital admission and up to eight discharge diagnoses.[18] Information on cause of death was obtained from the CDR.

2.2. Study population

A total of 77,536 men was diagnosed with PCa and for the present study, the inclusion criteria included: age under 80 at date of diagnosis, with high risk PCa defined as clinical local T3 tumour, and/or GS 8–10 and/or PSA 20–50 ng/mL, and date of diagnosis between January 1, 1997 and December 31, 2006 (Fig. 1). SES was available for 98.3% of all study subjects and the final study population consisted of 17,522 men.

2.3. Metastatic work-up, intention to treat, treatment modality and clinical subgroups

In the present study, a bone scan was judged to have been performed if the M-stage was recorded as M1 (metastatic disease)/M0 (no metastases) in the NPCR of Sweden. A treatment decision was defined both by the intention to treat approach and by either performed or planned curative treatment. Intention to treat was defined as either performed or planned curative treatment and/or performed lymph node dissection (N0/N1). In a subsequent step, the initial curative treatment was subdivided in radical prostatectomy or radiotherapy. Conservative treatment was defined as active surveillance, expectancy or hormonal treatment. The high risk PCa population was further subdivided into three clinical subgroups, based on local clinical tumour stage, PSA and GS as follows:

Group I: Local clinical T3 tumour or sPSA 20–50 ng/mL.
Group II: Local clinical T3 tumour and PSA 20–50 ng/m.L or GS 8–10 alone.
Group III: GS 8–10 and one or both of local clinical T3 tumour and PSA 20–50 ng/mL.

2.4. Socioeconomic status

Socioeconomic status was assessed by use of the Swedish Socioeconomic Index defined by Statistics Sweden.[19] The index is based on data from population and housing Censuses conducted between 1960 and 1990. The original Census consisted of 18 categories that defined the economically active population, primarily based on self-reported occupation. In subsequent Censuses, information on occupation was retrieved from the statement of earnings to the Swedish Tax Office. In the present study, the SES was aggregated into five categories based on occupation; blue-collar workers, farmers, self-employed, lower white-collar workers and higher white-collar workers. This SES is commonly used in epidemiological studies.[20,21] We used the last registered occupation since many patients were retired at the date of PCa diagnosis.

2.5. Co-morbidity

The Charlson Comorbidity Index was used to assess the burden of concomitant disease for each PCa patient.[22] The Charlson Comorbidity Index consists of an overall score, resulting in three co-morbidity levels; no (0), mild (1) and severe (2+), a categorisation that previously has been used in epidemiological studies.[23]

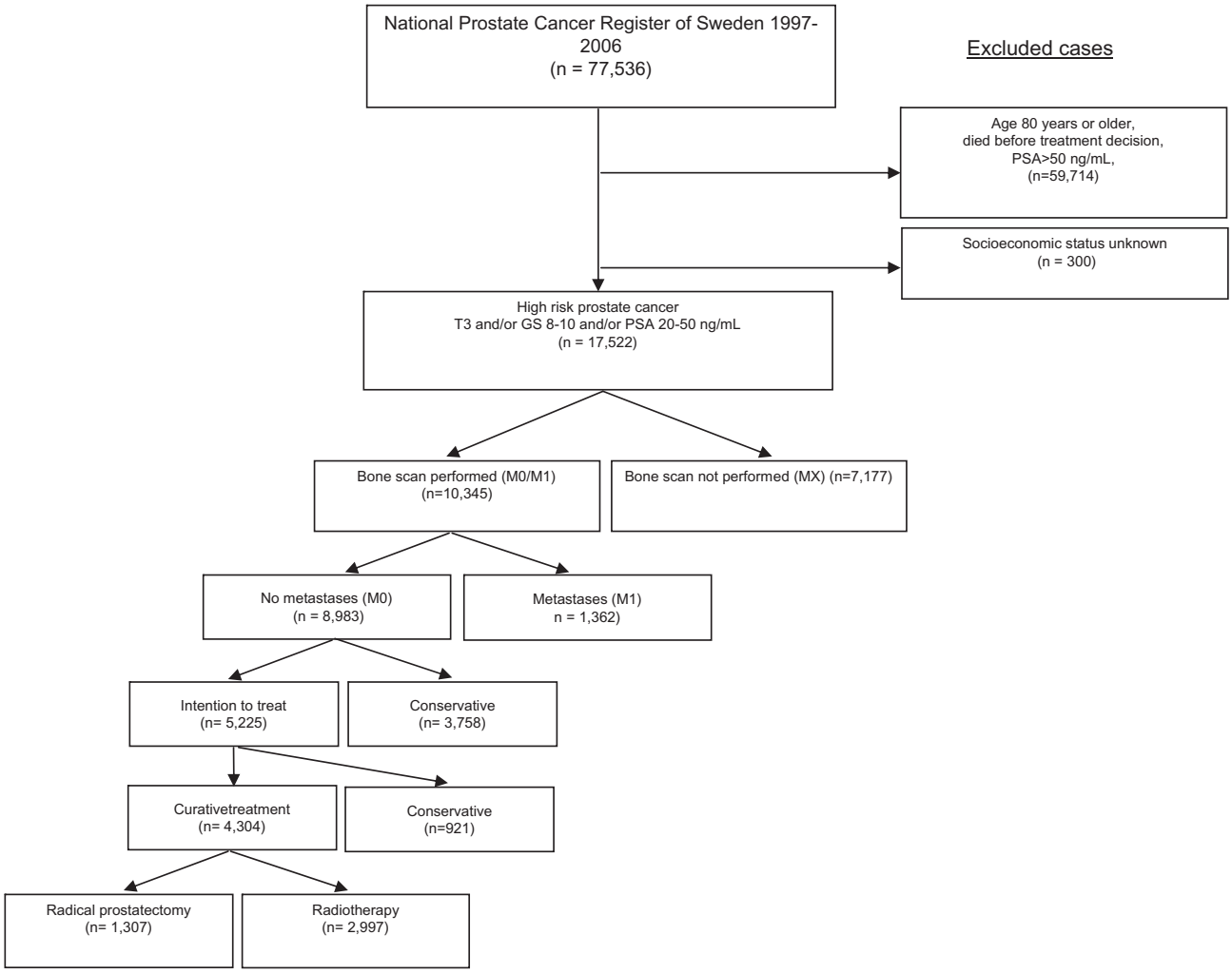

Fig. 1 – Flow chart of cohort assembly recorded in the National Prostate Cancer Register of Sweden between 1997 and 2006.

2.6. *Statistical methods*

In logistic regression models with odds ratios (OR) and 95% confidence intervals (CI), the likelihood to undergo a bone scan was examined in relation to SES following adjustment for comorbidity, age at diagnosis, calendar period and clinical subgroups. Logistic regression models were also used to assess whether intention to treat and curative treatment differed by SES following adjustment for co-morbidity, age at diagnosis, calendar period and clinical subgroups. In time to event analysis, the outcomes of interest were overall and PCa-specific mortality. Survival time was defined as the interval between the date of the PCa diagnosis and the date of the outcome, emigration or end of follow-up on December 31, 2007. In men without metastatic disease who either underwent or were planned to undergo curative treatment, we estimated cumulative probability of PCa-specific mortality by SES and stratified on type of treatment modality. In the same group of men who were free of metastases, Cox regression with hazard ratios (HR) were calculated to assess overall mortality in relation to SES, adjusted for age at diagnosis, calendar period, co-morbidity and clinical subgroups. To estimate PCa-specific mortality, Fine and Gray's competing risk regression with sub-distribution HR were used.[24] Finally, sensitivity analyses were conducted restricted to patients with no co-morbidity. All *p*-values were two-sided and statistical significance was considered at $p < 0.05$ and the analyses were performed using R 10.2.

The study was approved by the Central Ethics Committee at Umea University.

3. Results

3.1. *Socioeconomic status and patient characteristics*

Our study encompassed 17,522 patients. Of these, 6681 (38.1%) were blue-collar workers.

Amongst higher white-collar and blue-collar workers, 25.4% and 30.7% were 75 years or older at diagnosis, respectively. Amongst higher white-collar and blue-collar workers, 275 (9.6%) and 823 (12.3%) had severe co-morbidity, respectively.

Table 1 – Demographic, clinical characteristics, and socioeconomic status by diagnostic intensity in 17,522 patients diagnosed with high risk prostate cancer between 1997 and 2006 in the National Prostate Cancer Register of Sweden.

	Bone scan performed		Bone scan not performed		Total (*n*)
	n	%	*n*	%	
All	10,345	(59.0)	7177	(41.0)	17,522
Calendar period					
1997–1999	2977	(64.5)	1641	(35.5)	4618
2000–2002	3064	(59.8)	2063	(40.2)	5127
2003–2006	4304	(55.3)	3473	(44.7)	7777
Age at diagnosis					
<65	3030	(77.4)	883	(22.6)	3913
65–74	5189	(63.0)	3045	(37.0)	8234
75–79	2126	(39.6)	3249	(60.4)	5375
Clinical subgroups					
Group I	5083	(56.5)	3914	(43.5)	8997
Group II	2952	(60.0)	1969	(40.0)	4921
Group III	2310	(64.1)	1294	(35.9)	3604
Charlson comorbidity index					
CCI 0	7978	(62.0)	4881	(38.0)	12,859
CCI 1	1331	(53.2)	1173	(46.8)	2504
CCI 2+	1036	(48.0)	1123	(52.0)	2159
Socioeconomic status					
Blue-collar worker	3828	(57.3)	2853	(42.7	6681
Farmer	451	(51.7)	422	(48.3)	873
Self-employed	913	(58.8)	639	(41.2)	1552
Lower white-collar worker	3280	(59.2)	2263	(40.8)	5543
Higher white-collar worker	1873	(65.2)	1000	(34.8)	2873

3.2. *Socioeconomic status and work-up for metastatic status*

A bone scan (BS) was judged to have been performed in 10,345 (59%) of all men diagnosed with high risk PCa (Table 1). Metastatic disease was diagnosed in 412 (10.9%) higher white-collar workers and in 547 (14.3%) blue-collar patients. A social gradient was observed in that 65.2% of the higher white collar workers underwent BS compared to 57.3% of patients belonging to the blue-collar group. Following

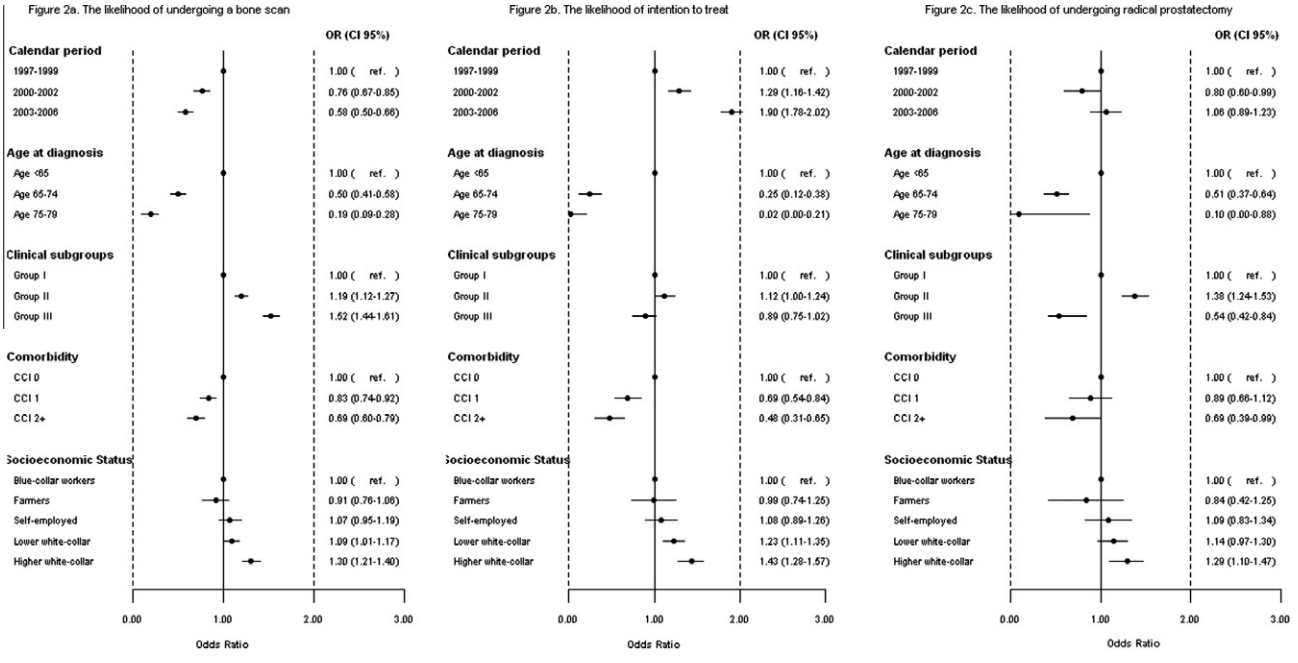

Fig. 2 – Likelihood of bone scan, intention to treat and radical prostatectomy in patients diagnosed with high risk prostate cancer diagnosed 1997–2006 in the National Prostate Cancer Register of Sweden.

Table 2 – Demographic, clinical characteristics and socioeconomic status by treatment modality in patients diagnosed with high risk prostate cancer determined free of metastatic disease following bone scan between 1997 and 2006 in the National Prostate Cancer Register of Sweden.

	Intention to treat		Conservative		Eligible patients[a] (*n*)	Radiotherapy		Radical prostatectomy		Eligible patients[b] (*n*)
	N	%	*n*	%		*n*	%	*n*	%	
All	5225	(58.2)	3758	(41.8)	8983	2997	(69.6)	1307	(30.4)	4304
Calendar period										
1997–1999	1235	(48.7)	1301	(51.3)	2536	644	(69.3)	285	(30.7)	929
2000–2002	1498	(56.4)	1159	(43.6)	2657	921	(73.4)	333	(26.6)	1254
2003–2006	2492	(65.8)	1298	(34.2)	3790	1432	(67.5)	689	(32.5)	2121
Age of diagnosis										
<65	2340	(86.3)	373	(13.7)	2713	1212	(61.3)	766	(38.7)	1978
65–74	2708	(59.4)	1845	(40.5)	4553	1681	(75.9)	534	(24.1)	2215
75–79	177	(10.3)	1540	(89.7)	1717	104	(93.7)	7	(6.3)	111
Clinical subgroups										
Group I	2726	(58.5)	1934	(41.5)	4660	1653	(70.3)	698	(29.7)	2351
Group II	1541	(60.4)	1012	(39.6)	2553	812	(63.4)	468	(36.6)	1280
Group III	958	(54.1)	812	(45.9)	1770	532	(79.0)	141	(21.0)	673
Charlson comorbidity index										
CCI 0	4367	(62.1)	2662	(37.9)	7029	2480	(68.7)	1129	(31.3)	3609
CCI 1	538	(47.7)	591	(52.3)	1129	313	(72.5)	119	(27.5)	432
CCI 2+	320	(38.8)	505	(61.2)	825	204	(77.6)	59	(22.4)	263
Socioeconomic status										
Blue-collar worker	1849	(56.4)	1432	(43.6)	3281	1080	(71.7)	426	(28.3)	1506
Farmer	177	(47.5)	196	(52.5)	373	264	(70.4)	111	(29.6)	375
Self-employed	449	(56.6)	344	(43.4)	793	111	(77.1)	33	(22.9)	144
Lower white-collar worker	1675	(58.4)	1193	(41.6)	2868	943	(69.1)	422	(30.9)	1365
Higher white-collar worker	1075	(64.4)	593	(35.6)	1668	599	(65.5)	315	(34.5)	914

[a] Eligible men are men diagnosed with high risk prostate cancer determined to be free of metastatic disease following a bone scan.
[b] Eligible men are men diagnosed with high risk prostate cancer determined to be free of metastatic disease following a bone scan that underwent curative treatment.

adjustment for age at diagnosis, calendar period, clinical subgroups and co-morbidity, a BS was significantly more likely to be offered higher white-collar compared to blue-collar workers (OR, 1.30; 95% CI, 1.21–1.40) (Fig. 2a).

3.3. Socioeconomic status and treatment modality

A total of 8983 patients with high risk PCa had no metastases. In an intention to treat approach amongst these men, 5225 (58.2%) were intended to undergo curative treatment (Table 2). The curative intent distribution amongst higher white-collar and blue-collar workers was 64.4% and 56.4%, respectively. Following adjustment potential confounders, patients with no metastases and with a higher white-collar work were more likely to receive curative treatment (OR, 1.43; 95% CI, 1.28–1.57) (Fig. 2b).

Amongst men with no metastases, 4304 (47.9%) underwent a curative treatment. In this group, higher white-collar workers were more likely to receive curative treatment after adjustment for prognostic factors (OR, 1.47; 95% CI, 1.35–1.59). Amongst these 4304 men free of metastases who were offered curative treatment, approximately two thirds (69.6%) received radiotherapy and one third underwent radical prostatectomy (Table 2). Following adjustment for potential confounders, higher white-collar workers were more likely to undergo radical prostatectomy (OR, 1.29; 95% CI, 1.10–1.47) (Fig. 2c).

3.4. Socioeconomic status and mortality

Amongst patients without metastases and who underwent curative treatment, the cumulative 10-year PCa-specific mortality was 10.0% (95% CI, 6.7–13.3%) amongst higher white-collar workers and 14.4% (95% CI, 11.2–17.8%) in blue-collar workers (Fig. 3). In the same subgroup and following adjustment for prognostic factors, a lower risk of PCa-specific mortality was observed in men with high white-collar work compared to blue-collar workers (sHR 0.70, 95% CI, 0.49–0.99) (Table 3). Amongst men that underwent curative treatment the risk of death from any cause was significantly lower in higher white-collar workers (HR, 0.76; 95% CI, 0.60–0.97).

4. Discussion

Our findings show that men with high SES more often underwent a more extensive work-up, received active treatment and had better outcomes compared to low SES men. Compared to blue-collar workers, higher white-collar workers were more likely to undergo bone scan, and to receive curative treatment, in particular radical prostatectomy, and had a lower overall and PCa mortality in the subgroup with no metastases that received curative treatment.

Strengths of our study included the population-based approach where the analyses were based on a nation-wide cohort including virtually all PCa patients diagnosed and managed in Sweden. The Swedish setting is characterised by a tax-funded National Health System used by virtually all residents with very limited care provided by private interests. Additional information was obtained from other register sources that allowed complete follow-up of all patients, including information on co-morbidity, which has been shown to be associated with management and outcomes in PCa patients.[23] Since mortality due to concomitant disease was more common than PCa death, competing risk analysis was appropriate.[25] Our study lacked information on marginal status in surgical specimen and no data were available on dose or fractionations in radiotherapy.[26–28] A bone scan was judged to have been performed if the M-stage was recorded as M1/M0. However, in earlier calendar years the manual to the registration stated that a morphological examination should be performed, and even though the overwhelming majority of examinations were bone scans, an unknown percentage of men underwent other examinations including CT-scan or plain radiography. Occupation is an established

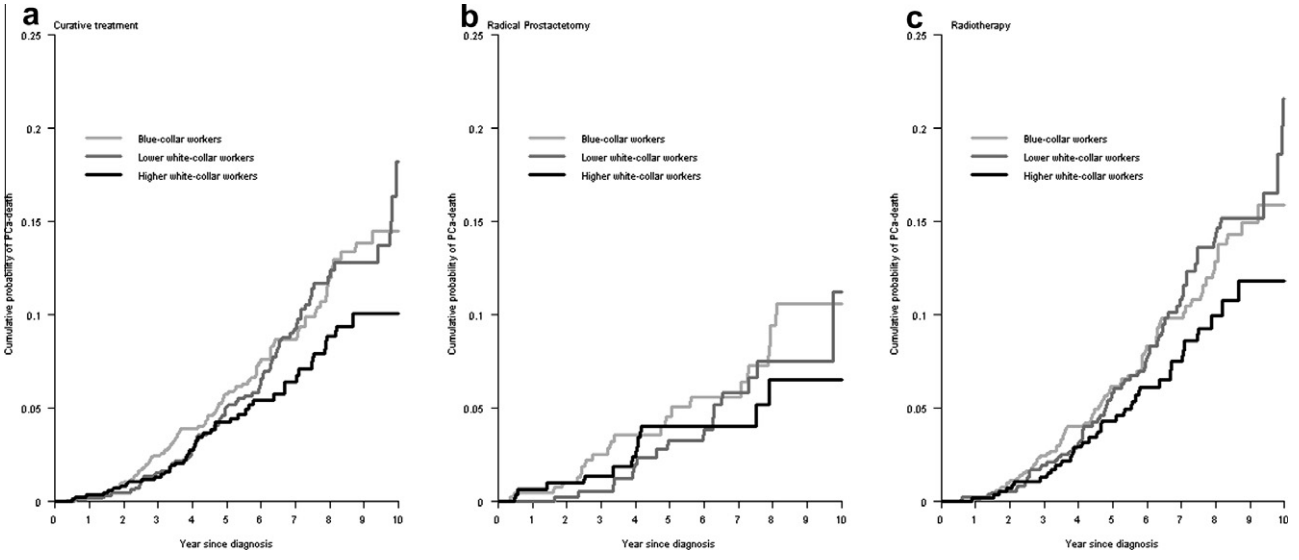

Fig. 3 – Cumulative probability of prostate cancer death by treatment and socioeconomic status in patients diagnosed with high risk prostate cancer.

Table 3 – Overall and cause-specific mortality using Cox and Fine and Gray's competing risk regression in patients diagnosed with high risk prostate cancer determined free of metastatic disease following a bone scan by treatment modality.

	Overall mortality						Cause-specific mortality					
	Curative		Radical prostatectomy		Radiotherapy		Curative		Radical prostatectomy		Radiotherapy	
	HR	(CI 95%)	HR	(CI 95%)	HR	(CI 95%)	sHR	(CI 95%)	sHR	(CI 95%)	sHR	(CI 95%)
Calendar period												
1997–1999	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)
2000–2002	0.97	(0.78–1.19)	1.00	(0.62–1.61)	0.95	(0.75–1.21)	0.84	(0.63–1.11)	1.22	(0.62–2.40)	0.76	(0.56–1.04)
2003–2006	0.96	(0.73–1.27)	1.09	(0.62–1.89)	0.92	(0.66–1.26)	0.75	(0.52–1.09)	1.32	(0.63–2.77)	0.62	(0.40–0.96)
Age of diagnosis												
<65	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)
65–74	1.29	(1.08–1.55)	1.48	(1.01–2.15)	1.19	(0.96–1.46)	0.76	(0.59–0.98)	0.97	(0.58–1.63)	0.66	(0.49–0.88)
75–79	2.15	(1.43–3.25)	3.14	(0.74–13.4)	1.88	(1.22–2.91)	1.75	(1.00–3.04)	3.30	(0.31–35.1)	1.41	(0.79–2.50)
Clinical subgroups												
Group I	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)
Group II	1.53	(1.26–1.85)	1.49	(0.91–2.45)	1.43	(1.16–1.77)	2.15	(1.61–2.87)	3.28	(1.76–6.11)	1.96	(1.41–2.73)
Group III	2.32	(1.63–3.29)	4.35	(1.73–10.9)	2.01	(1.37–2.94)	3.10	(2.27–4.24)	4.11	(1.84–9.17)	2.8	(1.99–3.94)
Charlson comorbidity index												
CCI 0	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)
CCI 1	1.43	(1.10–1.86)	1.24	(0.67–2.29)	1.46	(1.09–1.95)	1.21	(0.82–1.79)	1.48	(0.67–3.26)	1.12	(0.71–1.77)
CCI 2+	2.04	(1.54–2.71)	2.87	(1.60–4.13)	1.82	(1.32–2.52)	0.93	(0.54–1.61)	1.23	(0.37–4.04)	0.86	(0.46–1.59)
Socioeconomic status												
Blue-collar worker	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)
Farmer	0.68	(0.40–1.15)	0.82	(0.25–2.68)	0.65	(0.36–1.16)	0.87	(0.42–1.76)	0.62	(0.08–4.89)	0.93	(0.43–1.99)
Self-employed	0.72	(0.51–1.01)	0.68	(0.31–1.47)	0.72	(0.49–1.05)	0.73	(0.45–1.19)	1.11	(0.42–2.93)	0.64	(0.36–1.14)
Lower white-collar worker	0.86	(0.70–1.06)	0.75	(0.47–1.20)	0.90	(0.71–1.13)	0.93	(0.69–1.24)	0.71	(0.37–1.36)	1.03	(0.75–1.43)
Higher white-collar worker	0.76	(0.60–0.97)	1.07	(0.66–1.71)	0.68	(0.51–0.91)	0.70	(0.49–0.99)	0.68	(0.32–1.44)	0.73	(0.48–1.09)

indicator of SES,[29,30] but might not cover all aspects that contribute to the meaning of social status. The interpretation of results in some subgroups may have been hampered by a small number of events.

Since not all PCa patients have the same risk of developing bone metastases,[13] several studies have tried to identify patients for whom BS can be omitted.[31–33] However, in patients diagnosed with high risk PCa current guidelines on work-up recommend a BS.[34] In men for whom there is no curative intent, a BS is often omitted since it does not affect choice of treatment. Our finding that a higher proportion of high SES men underwent a BS may partly be explained by differences in clinical characteristics at diagnosis. However, the observed differences in diagnostic intensity remained after adjustment for clinical subgroups. In addition to clinical characteristics, symptoms, e.g. pain suggests the presence of metastasis and will justify the use of a bone scan. However, it appears unlikely that the prevalence of such symptoms systematically would be higher in white-collar patients. Hypothetically, our findings may reflect that higher SES men are more likely to report pain and other symptoms, compared to men with lower SES. It is also possible that patientś own preferences, in particular with regard to choice of treatment, differ between socioeconomic groups.

Ideally, the use of curative treatment should be determined by life expectancy and co-morbidity, i.e. biological age rather than by chronological age.[35] Our results indicate the presence of social differences both in the intention to treat approach and curative treatment. In addition to differences in co-morbidity and general health status, factors such as life-style, health care seeking behaviour and patient-clinician interactions may contribute to social variations in management. Curative treatment for men with localised high risk PCa is indicated given that life expectancy is estimated to be more than 5 years, but there are no randomised trials that have compared outcomes after radiotherapy and prostatectomy.[15] Corroborating our findings, results from several previous studies indicate that men with high SES are more likely to be offered surgery,[12,36] but none of these included information on co-morbidity. Despite adjustment for comorbidity in the present study, concomitant disease may have been both more common and more severe in low SES, ultimately influencing choice of treatment. Furthermore, patientś acceptance of risks associated with surgery may differ by SES.[37]

In men free of metastatic disease that either received or was planned to receive curative treatment, we observed a survival advantage for white-collar workers. Data in line with ours have been reported previously for men with low risk PCa,[38] and in studies without information on co-morbidity burden.[9] In a Swiss study, an elevated PCa-specific mortality risk was no longer present after adjustment for tumour characteristics and treatment.[9] Social variations in mortality may reflect factors associated with the tumour, the host and the Health Care System.

Tumour related factors, including a more advanced disease at time of diagnosis have been suggested as possible explanation for social inequalities in cancer survival.[11] However, it is notable that we observed no social differences with regard to the distribution of clinical subgroups.

Host related factors may partly explain the observed social differences in mortality. Life style factors like physical activity, nutritional status, overweight, tobacco and alcohol consumption, are related to SES,[39] and may affect outcome. In a recent Dutch study, cancer patients with low socioeconomic status had a substantially higher prevalence of co-morbid conditions. In that study, an estimated 22% of a social gradient in 1-year survival amongst PCa patients could be attributed to differences in co-morbidity burden.[40] In our study, the proportion of men with severe comorbidity was lower amongst white-collar compared to blue collar workers. We have recently reported of an increased overall and conditional PCa-specific mortality in patients with severe comorbidity, particularly in high risk PCa.[23] Importantly, in sensitivity analyses restricted to patients free of co-morbidity, we found essentially the same relationship between SES and mortality. However, a social gradient in mortality may reflect both host and treatment related factors, such as patient frailty, acceptance of treatment options and patient-doctor interactions.

The health care provider's attitude with regard to management may differ by SES. Our findings of more extensive work up and a higher frequency of intention to treat patients with higher SES may reflect aspects of physician- patient interaction and a subtle bias towards more action on behalf of the urologist when treating high SES men.

5. Conclusion

In conclusion, metastatic work-up, treatment and mortality in men with high risk PCa were influenced by SES within the setting of a tax-funded National Health Care System aiming to provide care to residents on equal terms. In addition to the observed differences in co-morbidity burden, several factors that are potentially modifiable may contribute to our findings including unequal access to care, life-style factors, patients' preferences and patient-clinician interactions. The pattern of management and mortality in the most affluent groups should represent a minimum standard for all prostate cancer patients. It cannot be excluded that social inequalities in management and outcomes may be even more pronounced in regions with more heterogeneous Health Care Systems and larger socioeconomic gradients than in Sweden.

Conflict of interest statement

All authors have no disclosures to report, including any financial, personal or other relationships with other people or organizations within that could inappropriately influence their work.

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