Educational inequalities in cancer survival: a role for comorbidities and health behaviours?

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► Additional supplementary tables are published online only. To view these files please visit the journal online (http://dx.doi.org/10.1136/jech-2012-201404)

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Received 18 April 2012
Revised 31 October 2012
Accepted 7 November 2012
Published Online First 8 December 2012

To cite: Aarts MJ, Kamphuis CBM, Louwman MJ, *et al. J Epidemiol Community Health* 2013;**67**:365–373.

ABSTRACT

Aim To describe educational inequalities in cancer survival and to what extent these can be explained by comorbidity and health behaviours (smoking, physical activity and alcohol consumption).

Methods The GLOBE study sent postal questionnaires to individuals in The Netherlands in 1991 resulting in 18 973 respondents (response 70%). Questions were asked on education, health and health-related behaviours. Participants were linked for cancer diagnosis (1991–2008), comorbidity and survival (up to 2010) with the population-based Eindhoven Cancer Registry; 1127 tumours were included in the analyses.

Results 5-year crude survival was best in highly educated patients as compared with low educated patients for all cancers combined: 49% versus 32% in male subjects (log rank: p<0.0001), 65% versus 49% in female subjects (p=0.0001). Compared with highly educated, low educated prostate cancer patients had an increased risk of death (HR 2.9 (95% CI 1.7 to 5.1), adjusted for age, stage and year). No or inconsistent associations between educational level and risk of death were seen in multivariable analyses for breast, colon and non-small cell lung cancer. Although survival in prostate cancer patients was affected by comorbidities ($HR_{2\_vs\_0\_comorbidities}$: 2.6 (1.5 to 4.4)), physical activity ($HR_{no/little\_vs\_\_moderate\_physical\_\_activity}$: 2.0 (1.2 to 3.4)) and smoking ($HR_{current\_vs\_never\_smokers}$: 2.6 (1.0–6.8)), these did not contribute to educational inequalities in prostate cancer survival ($HR_{low\_vs\_high\_education}$: 3.1 (1.6 to 5.8) with adjustment for comorbidity and lifestyle).

Conclusions Compared with low educated, highly educated prostate cancer patients had better survival. Although presence of comorbidities, physical activity levels and smoking status affected survival from prostate cancer, these did not contribute to educational inequalities in survival. The role of other factors for inequalities in cancer survival needs to be explored.

INTRODUCTION

Many studies report the highest cancer mortality rates among those with low socioeconomic position (SEP).[1–4] This disadvantage may be the result of higher cancer incidence in low SEP groups. Indeed, people from lower socioeconomic strata have more or less consistent excess risks for respiratory cancers, cancers of the head and neck and upper gastrointestinal tract, liver and cervix uteri.[1 5–7] Risks for cancers of the colon, breast and ovary and malignant melanoma are generally lower in those with a low SEP,[1 5–7] which are likely related to socioeconomic differences in unhealthy behaviours. Part of the increased risks of developing lung and breast cancer can be explained by smoking, alcohol intake and physical activity.[8] Recently, smoking was thought to explain 19% of all new cancer cases in the UK, whereas deficient intake of fruits and vegetables, occupational exposures, overweight and obesity and infectious agents explained 4%–7% of cancer incidence.[9]

Increased cancer mortality rates among people with lower SEP may result from increased incidence and poorer survival from cancer. Survival rates from cancer are generally better for patients with high SEP,[4 5 10–12] which has been ascribed partly to lower prevalence of other chronic diseases (comorbidities) in high SEP cancer patients.[13 14] The presence of these comorbidities is affected by lifestyle (eg, smoking is related to the occurrence of chronic obstructive pulmonary disease (COPD) and cardiovascular disease), and lifestyle likely influences the socioeconomic inequalities in cancer survival as well. Because unhealthy behaviours are not necessarily reflected in quantifiable comorbidity scores, lifestyle may further explain socioeconomic inequalities in cancer survival. Previous studies on this topic reported small effects of smoking, physical activity and alcohol consumption upon socioeconomic differences in survival from respiratory-related cancers, colorectal cancers and all cancers combined in New Zealand and Sweden.[15 16] The explanatory role of lifestyle in socioeconomic inequalities in cancer survival has not been studied for other cancers separately nor the additional effect of comorbidities. The aim of our study is to describe educational inequalities in cancer survival and to what extent these inequalities can be explained by comorbidity and lifestyle factors.

The prospective GLOBE study was designed to investigate several explanations for socioeconomic inequalities in health in The Netherlands. Linkage of information from study participants to the Eindhoven Cancer Registry enabled us to study the presence of socioeconomic inequalities in cancer survival and the contribution of three cancer-related behavioural risk factors (alcohol consumption, smoking and physical activity) and comorbidities.

METHODS

Population

The prospective cohort, that is, the Dutch GLOBE study, started in 1991, and aimed to investigate the contribution of explanatory factors to socioeconomic inequalities in health. GLOBE is the Dutch acronym for 'Health and Living Conditions of the Population of Eindhoven and Surroundings'. A detailed description of the purpose and design of the GLOBE study, and the main results after the first 10 years are presented elsewhere.[17 18] In short, in 1991 a postal questionnaire was sent to non-institutionalised Dutch persons between 15 and 75 years of age, living in or near the city of Eindhoven, to which 18 973 individuals responded (70.1%). The questionnaire included measures of SEP, self-reported health, health-related behaviour (eg, smoking, alcohol consumption, physical activity), material circumstances (housing, income), psychosocial characteristics (marital status, vitality), healthcare utilisation and childhood circumstances.

Cancer survival

The population-based Eindhoven Cancer Registry has collected data on new cancer patients since 1955 according to international guidelines.[19] Trained registry personnel actively collects data on diagnosis, staging and treatment. Stage was divided according to Tumour Node Metastasis (TNM) classification at the year of diagnosis, according to the fourth, fifth and sixth International Union Against Cancer editions, as appropriate.[20–22] Pathological T, N and M stages were used; clinical stage was used if pathological stage was missing. In prostate cancer, we used the clinical stage. Clinical TNM stage was determined by physical examination, imaging, endoscopy, biopsy, surgical exploration and other relevant examinations. Pathological TNM stage was based on the evidence acquired before treatment, supplemented or modified by the additional evidence acquired from surgery and from pathological examination.

The registry also records serious comorbidity at diagnosis according to an adaptation of the list of Charlson and coworkers.[23] An overview of the comorbidities associated with the various cancer sites in relation to SEP is given elsewhere.[13]

Since 1988, the registry has covered an area in the south-east of The Netherlands with a population of over 2 million inhabitants, including the area in which GLOBE participants resided. Information on vital status of the patients was obtained from the population registries network, which provides virtually complete coverage of all deceased citizens of The Netherlands. Follow-up was complete for cancer patients until 31 December 2009. Non-cancer patients who moved out of the area were lost to follow-up. Data on cause of death were not available in this study.

Questionnaire information from respondents and cancer registry records were linked in a two-step procedure. First, a combination of the respondent's sex, date of birth and the first two characters of his or her last name at birth were used as a linking key. In a second step, uncertain matches were checked by visual inspection of the Eindhoven Cancer Registry, using identifiable data (such as initials, full last names and address). We included patients diagnosed from 1991 to 2008. Patients who indicated in the questionnaire that they had suffered from 'malignant disease or cancer' in the past were excluded from the present study (n=70, mainly cancers of the breast, colon and lung and basal cell carcinomas), as patients could have changed to a more healthy lifestyle in response to their disease. Survival rates are only shown if at least five patients were at risk of dying per subgroup for any given time since diagnosis. We studied four common cancers: patients with colon and non-small cell lung cancer, male subjects with prostate cancer, and female subjects with breast cancer. In the analyses of all cancers combined, basal cell carcinomas were excluded since these have very low lethality. Furthermore, in case a patient had more than one tumour, we only included the first cancer.

Educational level

Educational level was indicated by the highest attained level of education with students classified according to their current training, using a closed question in the baseline questionnaire. Four different groups were created: (1) primary school only; (2) lower vocational school and lower secondary school; (3) intermediate vocational school and intermediate/higher secondary school; and (4) higher vocational school and university. In The Netherlands, educational level is recognised as a good indicator of SEP.[24] The highly educated group was used as the reference group.

Behavioural variables

Self-reported current smoking behaviour was categorised into four groups: never, former smoker, current smoker and unknown. On the basis of questions on the average number of days per week that individuals used alcohol and the average number of glasses consumed per day, individuals were categorised into five groups for alcohol consumption: total abstainers; light; moderate; excessive; and unknown drinkers (for details see[25]). Leisure physical activity was calculated from the number of hours spent on gardening, cycling, walking and physical exercise (none or little; moderate; much; unknown, for details see[26]).

Survival analyses

Crude survival analyses were performed using the Kaplan–Meier method, and comparisons between groups assessed by the log rank test. Cox proportional regression analyses were performed to assess the effects of comorbidities and behavioural variables on risk of death. We first adjusted for age categories (0–59, 60–69 and 70 years and older), period of diagnosis (1991–1996, 1997–2002 and 2003–2008) and stage at diagnosis. Subsequently we adjusted for presence of comorbidities, categorised into: 0; 1; 2 or more; unknown. We additionally added alcohol, physical activity and smoking, resulting in the final model. The comparisons of models with different covariates were tested with the likelihood ratio test.

RESULTS

Between 1991 and 2008, 2576 first primary tumours were diagnosed within the GLOBE population of 18 973 individuals (table 1). The percentage of patients with a low educational level varied considerably per tumour localisation; 41% of male small cell lung cancer patients and 39% of female patients with non-melanoma skin cancer or with unknown primary localisation only attended primary school, compared with 19% and 18% of the male and female melanoma patients. Survival was best in patients with a high educational level, in both male and female subjects (figure 1). Crude 5-year survival for all cancers combined (ie, all cancers as presented in table 1) was 49% in male subjects with high educational level compared with 32% in low education (log rank: $p<0.0001$), and 65% and 49% in female subjects ($p=0.0001$), respectively (see figure 1).

Subsequent analyses were only performed on patients with known educational level and with breast (female subjects only, n=356), colon (n=226), prostate (n=271) or non-small cell lung cancer (n=274). These 1127 tumours were present in 1096 patients. In prostate cancer, patients with low educational level had poorer survival (log rank: $p=0.0002$), while crude survival from colon cancer and non-small cell lung cancer was the lowest in highly educated patients (figure 1, $p=0.2$ and 0.5, respectively). Breast cancer survival was best in highly educated women (5-year survival 87%) and poorest in low educated women (69%, $p=0.2$).

No consistent socioeconomic patterns were present in mean age or stage distribution of the cancer patients (data not shown).

Table 1 Percentage of patients by tumour site (10 most common and basal cell carcinoma) and educational level, patients in the longitudinal GLOBE study, Eindhoven, The Netherlands, diagnosed 1991–2008

		Educational level				
	Total N	1. Low %	2. %	3. %	4. High %	Other/ unknown %
Males						
Oesophagus (including cardia stomach)	46	20	48	11	17	4
Colon	127	20	29	28	19	3
Rectum	62	27	34	16	19	3
Non-small cell lung cancer	225	35	30	20	8	6
Small cell lung cancer	69	41	36	10	13	0
Skin, melanoma	52	19	25	21	35	0
Skin, non-melanoma (SCC*)	69	28	29	19	20	4
Prostate	286	25	26	21	23	5
Urinary bladder	107	32	22	24	20	3
Primary localisation unknown	46	33	22	22	17	7
Total (excluding basal cell carcinoma)	*1435*	*27*	*30*	*21*	*18*	*4*
Skin, basal cell carcinoma	186	25	28	19	23	5
Females						
Colon	115	32	40	10	7	10
Rectum	40	35	38	20	3	5
Pancreas	26	35	54	12	0	0
Non-small cell lung cancer	65	34	49	12	0	5
Skin, melanoma	38	18	58	18	5	0
Skin, non-melanoma (SCC)	44	39	48	7	2	5
Breast	371	26	51	15	5	4
Corpus uteri	60	37	48	7	8	0
Ovary	39	23	44	18	13	3
Primary localisation unknown	41	39	37	5	10	10
Total (excluding basal cell carcinoma)	*1141*	*31*	*47*	*13*	*5*	*5*
Skin, basal cell carcinoma	161	25	45	21	2	7

*SCC, squamous cell carcinoma.

The prevalence of comorbidities was slightly higher among low educated cancer patients (table 2). Furthermore, among the low educated patients, a higher proportion smoked and did not drink any alcohol. Levels of physical activity were the highest among the highest educated. Crude survival from colon, prostate and breast cancer was better among patients with no or, in case of prostate and breast cancer, one comorbidity than with two or more comorbidities, with 11% higher 3-year survival in colon cancer patients with no comorbidities compared with patients with two or more comorbidities (p value log rank test: 0.0015), 21% in prostate ($p=0.0004$) and 8% in breast cancer ($p=0.0012$). Furthermore, crude survival was better in prostate and breast cancer patients with high compared with low levels of physical activity (31% higher in prostate ($p=0.0167$), 2% in breast ($p=0.0454$)) (table 3). Among prostate and breast cancer patients, survival was better for those with light or excessive alcohol consumption than for total abstainers or moderate consumers, although none of these associations were statistically significant.

In multivariable models adjusting for age, year of diagnosis and stage at diagnosis, risk of death in prostate cancer patients was higher for those with low compared with high education, although with wide CIs ($HR_{low\_vs\_high\_educated}$ 2.9 (95% CI 1.7 to 5.1) see table 4). Associations of education with risk of death among breast, colon and non-small cell lung cancer patients were inconsistent and non-significant after adjustment for age, year of diagnosis and stage at diagnosis.

In multivariable models for prostate cancer as presented in table 5, poor survival was predicted by presence of comorbidities ($HR_{2\ or\ more\ vs\ no\ comorbidities}$: 2.6 (1.5 to 4.4)), low levels of physical activity ($HR_{no/little\ vs\ moderate\ physical\ activity}$: 2.0 (1.2 to 3.4)) and being a current smoker ($HR_{current\ vs\ never\ smokers}$: 2.6 (1.0 to 6.8)). The increased hazard of death in low educated prostate cancer patients compared with the highly educated patients (model A, $HR_{low\_vs\_high\_educated}$: 2.9 (1.7 to 5.1), table 4) hardly changed by inclusion of comorbidities ($HR_{low\_vs\_high\_educated}$: 2.7 (1.6 to 4.8), table 5), lifestyle behaviours ($HR_{low\_vs\_high\_educated}$: 3.0 (1.6 to 5.6)) or both in the model ($HR_{low\_vs\_high\_educated}$: 3.1 (1.6 to 5.8)). In contrast to lifestyle behaviours, adding comorbidity to the model leads to a significantly better fit of the data (likelihood ratio test model A +comorbidity compared with model A: $p<0.01$).

Survival of colon, breast and non-small cell lung cancers was not associated with educational level and associations remained of similar magnitude after inclusion of comorbidities and/or lifestyle behaviours in the multivariable models (see online supplementary tables S1, S2, S3A, S3B and S4).

DISCUSSION

In this study, we investigated educational differences in cancer survival and the contribution of comorbidity and lifestyle to survival. In all cancers combined and prostate cancer patients separately, those with high education had the best survival. In contrast, risks of death were inconsistently or not related to education in colon, breast and non-small cell lung cancer. Although comorbidity and lifestyle behaviours predicted death in prostate cancer patients, these could not explain the increased risk of death in low educated prostate cancer patients.

Our results confirm previous studies that also pointed to better survival for patients with high SEP for prostate cancer, while our findings are not in line with associations previously reported for breast, colon and lung (which will be discussed later).[4 5 11 12 14 27] Not surprisingly, the difference between high and low SEP in survival was limited for lung cancer, which is rather lethal and the effects of comorbidities and lifestyle are expected to be minor. Contrasting our expectations, crude survival was lower in highly educated non-small cell lung cancer patients than in low educated, although not significantly. These probably relate to differences in comorbidities and age, since hazards of death were not significantly related to education in the multivariable analyses.

The reasons for socioeconomic inequalities in cancer survival are not exactly known yet, but differences in stage at diagnosis, treatment and lifestyle-related factors such as physical activity, obesity and dietary patterns have been proposed. Some previous studies took into account stage at diagnosis, which was reported not to fully explain better survival in high SEP patients with prostate (depending on age), breast (only in screen-detected tumours) and in some studies on colorectal cancer.[4 11 14 27] We also observed a strong significant effect of stage on survival, but it did not explain all of the educational inequalities in prostate cancer survival. In addition, excluding stage from the age and year adjusted model only little increased the HR for low compared with high educated patients

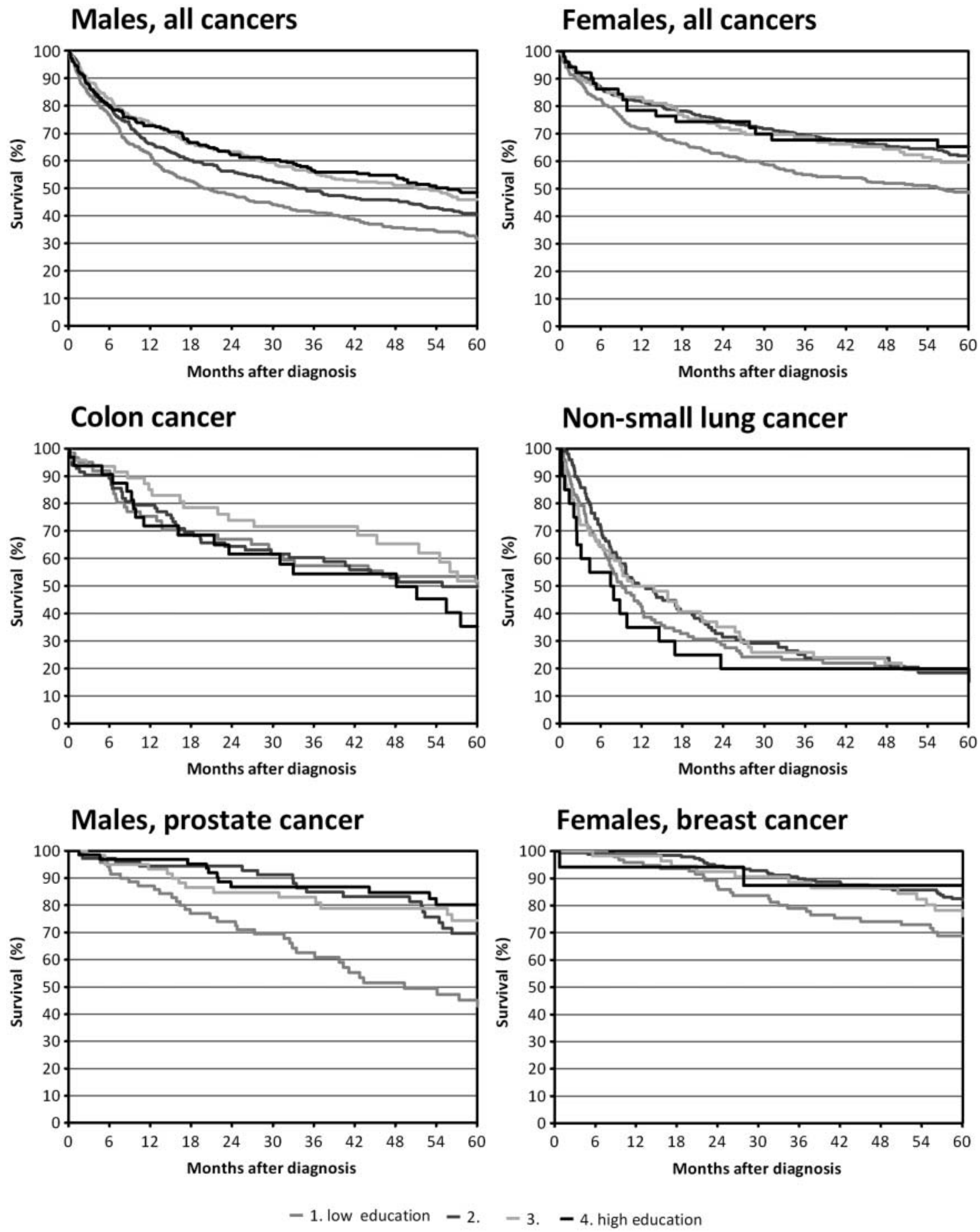

Figure 1 Crude survival from cancer by tumour site and sex, according to educational level, patients in the longitudinal GLOBE study, Eindhoven, The Netherlands, diagnosed 1991–2008.

(data not shown). Also unsurprisingly, age was strongly related to survival.

In our analyses we furthermore adjusted for presence of comorbidities at diagnosis, and investigated the additional effects of alcohol consumption, physical activity and smoking on educational inequalities in cancer survival. We assumed that by adjusting for comorbidity we also adjusted partly for lifestyle. Comparing the models with comorbidity, behaviour and the final model shows that associations of lifestyle hardly changed by inclusion of comorbidity and vice versa (see online supplementary tables S1, S2, S3A, S3B and S4, likelihood ratio test for all comparisons not significant). This may suggest that comorbidities reflect high-risk behaviours well.

Previously we have shown that comorbidities explained some of the socioeconomic variation in breast, colorectal and prostate cancer survival.[13 14 27] Although comorbidity was reported to be a significant prognostic factor in cancer,[28] it did not explain the educational difference in prostate cancer survival in our study. We expect this to result from the rather weak association between education and comorbidities.

Furthermore, differences in treatment between socioeconomic groups may contribute to the socioeconomic inequalities in

Table 2 Distribution of comorbidity at diagnosis and behaviours at baseline (1991) by educational level in the longitudinal GLOBE study, Eindhoven, The Netherlands, including patients with prostate, non-small cell lung, colon and breast cancer, diagnosed 1991–2008

	Educational level				
Number of tumours	1. Low 330 (%)	2. 443 (%)	3. 219 (%)	4. High 135 (%)	p Value*
Comorbidities					
None	27	43	35	39	0.0006
1	26	26	29	27	
2 or more	35	21	23	23	
Unknown	12	10	13	11	
Smoking					
Never	25	24	18	13	<0.0001
Former	25	33	39	55	
Current	46	41	41	33	
Unknown	5	2	2	0	
Alcohol					
Total abstainers	37	21	11	8	<0.0001
Light	33	45	39	39	
Moderate	12	19	32	42	
Excessive	8	9	14	7	
Unknown	11	6	4	4	
Physical activity					
None/little	21	19	15	11	<0.0001
Moderate	58	56	49	50	
Much	14	23	32	37	
Unknown	8	2	4	2	

*p Values are from χ^2 test.

Table 3 Crude survival according to number of comorbidities at diagnosis and behaviours at baseline (1991) per tumour site in the longitudinal GLOBE study, Eindhoven, The Netherlands

	Colon	Non-small cell lung	Prostate	Breast
Mean age at diagnosis	**70.4**	**66.4**	**70.1**	**63.5**
	3-year survival (%)	**1-year survival (%)**	**3-year survival (%)**	**3-year survival (%)**
Comorbidities at diagnosis				
None	69	41	85	88
1	53	49	84	86
2 or more	58	45	64	80
Unknown	68	55	83	87
Smoking				
Never	62	*	81	87
Former	63	52	80	84
Current	58	45	76	87
Unknown	*	*	86	92
Alcohol				
Total abstainers	64	45	69	83
Light	67	45	82	90
Moderate	54	38	79	80
Excessive	55	57	90	94
Unknown	50	63	67	88
Physical activity				
None/little	80	47	57	88
Moderate	57	48	82	85
Much	57	38	88	90
Unknown	56	50	*	64

Includes patients with prostate, non-small cell lung, colon and breast cancer, diagnosed 1991–2008.
*Less than five patients in this group; data not shown.

cancer survival. Unfortunately, small numbers of patients receiving each therapeutic option hampered inclusion in multivariable analyses. However, since we adjusted for clinical stage in our analyses, and since treatment is related to stage (as we expect patients with more advanced stages of cancer to receive other types of treatment than those with less severe stages), additional adjustment for treatment is not likely to substantially change our results.

Few studies investigated the role of lifestyle in socioeconomic inequalities in cancer survival. A Danish study showed that comorbidity, and to a lesser extent lifestyle, were influencing the socioeconomic variation in colorectal cancer survival, while factors related to disease or treatment were not contributing to the variation.[29] Also smoking status prior cancer diagnosis was an important predictive factor for socioeconomic variation in cancer survival in Norwegian women, whereas in breast cancer no association with smoking status, alcohol consumption, stage or comorbidity was found.[30] In men smoking and alcohol consumption did not explain socioeconomic variation in Swedish overall cancer survival.[15] In New Zealand, socioeconomic variation in colorectal cancer survival could not be explained by smoking status, alcohol intake and physical activity.[16] Previously the role of alcohol was suggested to substantially influence socioeconomic inequalities in male cancer mortality (being the product of incidence and survival) in some, but not other European countries.[31] The Netherlands was not taken into account.

Other factors that could contribute to the better survival in highly educated cancer patients are healthier lifestyle in general (other than we could measure). Furthermore, those with high SEP have generally better capacity to obtain, process and understand health information and services (the so-called 'health literacy').[3 32] These socioeconomic differences in health literacy could have contributed to better cancer survival among highly educated prostate cancer patients.

For prostate cancer we stratified the analyses according to tumour stage to unravel possible screening effects. Overall, results were similar to the total group of prostate cancer patients. Compared with those with advanced stage, effects of smoking and physical activity were stronger in those with localised disease (see online supplementary table S3A and S3B). Presence of comorbidities strongly affected risk of death in those with advanced disease (≥2 compared with no comorbidities: HR 4.8 (95% CI 1.7 to 13.8)).

Prostate cancer survival might have also been influenced by the increased use of prostate specific antigen (PSA) tests, which occurred mainly from 2000 onwards.[33–35] It has been reported that PSA testing occurs more often in male subjects with high compared with low SEP.[36] However, by adjusting for tumour stage at diagnosis we aimed at taking at least part of these socioeconomic differences in staging into account.

Relatively small studies like GLOBE take a long time to answer questions on socioeconomic inequalities in survival of specific types of cancer. A systematic approach to study these inequalities is important, and cancer registries could play an important role in these studies.

Table 4 Multivariable risk of death according to tumour site for cancer patients in the longitudinal GLOBE study, Eindhoven, The Netherlands, diagnosed 1991–2008

	Colon		Non-small cell lung		Prostate		Breast	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Age								
0–59	1.0		1.0		1.0		1.0	
60–69	1.7	0.8 to 3.7	**2.1**	1.4 to 3.1	2.0	0.7 to 5.2	1.3	0.8 to 2.1
70+	1.9	0.9 to 4.1	**2.6**	1.7 to 3.9	**5.0**	1.6 to 12.7	**2.5**	1.5 to 4.0
Sex								
Female	1.0	0.6 to 1.4	1.0	0.7 to 1.4	–		–	
Male	1.0		1.0					
Year of diagnosis								
1991–1996	1.0	0.6 to 1.7	**1.5**	1.0 to 2.2	1.0	0.0 to 1.9	0.8	0.4 to 1.4
1997–2002	1.4	0.9 to 2.2	**1.5**	1.1 to 2.1	1.3	0.2 to 2.1	1.1	0.6 to 1.9
2003–2008	1.0		1.0		1.0		1.0	
Stage								
1	1.0		1.0		1.0		1.0	
2	1.0	0.5 to 1.9	**2.7**	1.4 to 5.5	1.0	0.0 to 2.0	**2.0**	1.3 to 3.1
3	**1.9**	1.0 to 3.6	**2.9**	2.0 to 4.3	1.2	0.2 to 3.0	**2.6**	1.4 to 4.9
4	**8.4**	4.4 to 16.1	**5.9**	3.8 to 9.0	**4.0**	1.4 to 7.8	**10.8**	5.0 to 23.2
Unknown	**20.7**	7.7 to 56.1	1.3	0.8 to 2.1	**4.4**	1.5 to 11.3	1.1	0.2 to 8.4
Education								
1. Low	1.1	0.6 to 1.9	0.8	0.5 to 1.3	**2.9**	1.7 to 5.1	1.5	0.5 to 4.4
2.	0.7	0.4 to 1.2	0.7	0.4 to 1.2	1.5	0.4 to 2.6	1.3	0.4 to 3.5
3.	0.7	0.3 to 1.2	0.8	0.5 to 1.5	1.6	0.5 to 3.0	1.4	0.5 to 4.3
4. High	1.0		1.0		1.0		1.0	

Values in bold are significant. Models are adjusted for all variables listed.

Our study findings might be influenced by several methodological limitations. We have excluded subjects with prevalent cancer at baseline (ie, 1991) in order to eliminate possible selection effects. The validity of the self-reported prevalence of cancer in the study population that filled in the 1991 questionnaire was checked, and some under-reporting was found among those with a lower educational level.[37] Furthermore, we assumed that lifestyle prior to cancer diagnosis was indicative to lifestyle after diagnosis. However, this can be debated as the experience of cancer diagnosis and treatment may serve as a critical cue for an individual to make positive health behaviour changes.[38] Also the small number of patients within each group, which is reflected by the wide CIs, is a serious weakness of our study. This may explain the rather unusual results for colon, breast and non-small lung cancer survival, which was not associated with education. Unfortunately, we were only able to calculate overall survival, since no SEP-specific life tables were available to estimate cancer specific survival according to SEP.

Reporting of smoking habits, alcohol consumption and physical activity may be inaccurate and is often understated or overstated in case of physical activity, although a recent study reported that this was not true for nicotine consumption.[39–41] Reporting on these items may differ across the SEP groups, thereby introducing differential bias. This may dilute the effect of lifestyle and may (partly) explain why lifestyle hardly affected the educational differences in cancer survival.

A disadvantage of using education is that it better reflects SEP in some age cohorts than in others.[42] Those born before 1950 may not have attained the educational level that could be expected based on their potential abilities. This effect is probably stronger for women. The effect of possible misclassification of SEP by using educational level may explain why our results are not in accordance with previous studies on SEP and cancer survival and on the prevalence of comorbidities and SEP, which explained part of the inequalities in cancer survival.[13 14] Besides, it may also explain the rather uncommon finding of relatively few highly educated women with breast cancer. However, we previously reported no consistent pattern for breast cancer incidence with SEP for all ages combined, but high incidence rates in elderly women with low SEP.[7] Because a large proportion of the breast cancer patients in our study is relatively old, it may explain higher breast cancer incidence rates in women with low education.

Nevertheless, comparison of the educational level with fiscal data on household income and value of housing[43] shows a fair correlation.

A strength of this study is that the follow-up of the original sample on vital status has been nearly complete (99.8%). Additionally, the completeness of the Eindhoven Cancer Registry is expected to be at least 95%;[44] thus, only few new cancer cases diagnosed within the registration area would not be included in the cancer registry. Furthermore, the area covered by the Eindhoven Cancer Registry is much larger than the area covered by the GLOBE study, so participants who moved outside the area of the GLOBE study, but still within the area of the Eindhoven Cancer Registry, could also be included in the present study. Those moving outside the GLOBE study area were in a previous study found to be mainly highly educated individuals with few comorbidities and high levels of physical activity, which might have influenced our results. However, these were mostly young individuals who have a low chance of developing cancer.[45] Finally, the two-step linkage procedure

Table 5 Multivariable risk of death for prostate cancer patients in the longitudinal GLOBE study, Eindhoven, The Netherlands, diagnosed 1991–2008

	Model A+comorbidity		Model A+lifestyle behaviours		Model A+comorbidity +lifestyle behaviours	
	HR	95% CI	HR	95% CI	HR	95% CI
Age						
0–59	1.0		1.0		1.0	
60–69	1.8	0.7 to 4.7	2.4	0.9 to 6.4	2.1	0.8 to 5.7
70+	**3.9**	1.5 to 10.1	**5.8**	2.2 to 15.5	**4.7**	1.7 to 12.6
Year of diagnosis						
1991–1996	1.4	0.7 to 2.6	1.0	0.5 to 1.7	1.3	0.7 to 2.4
1997–2002	1.3	0.8 to 2.2	1.2	0.7 to 2.1	1.3	0.8 to 2.2
2003–2008	1.0		1.0		1.0	
Stage						
1	1.0		1.0		1.0	
2	1.4	0.7 to 2.8	0.9	0.5 to 1.9	1.3	0.6 to 2.6
3	1.6	0.6 to 4.2	0.9	0.4 to 2.3	1.3	0.5 to 3.3
4	**6.0**	2.9 to 12.1	**3.7**	1.9 to 7.3	**5.4**	2.6 to 11.1
Unknown	**5.9**	2.3 to 15.3	**4.8**	1.8 to 12.6	**6.5**	2.5 to 17.4
Education						
1. Low	**2.7**	1.6 to 4.8	**3.0**	1.6 to 5.6	**3.1**	1.6 to 5.8
2.	1.4	0.8 to 2.5	1.4	0.8 to 2.5	1.4	0.8 to 2.6
3.	1.6	0.9 to 2.9	1.6	0.9 to 2.9	1.5	0.8 to 2.8
4. High	1.0		1.0		1.0	
Comorbidities						
0	1.0				1.0	
1	1.5	0.9 to 2.5			**1.8**	1.0 to 3.0
2 or more	**2.6**	1.5 to 4.4			**3.0**	1.7 to 5.1
Unknown	1.2	0.6 to 2.5			1.8	0.8 to 3.7
Alcohol						
Abstainer			0.9	0.5 to 2.0	0.9	0.4 to 1.9
Light			1.0	0.6 to 1.7	1.1	0.6 to 1.7
Moderate			1.0		1.0	
Excessive			1.3	0.6 to 2.8	1.3	0.6 to 2.8
Unknown			1.6	0.6 to 4.0	1.7	0.7 to 4.4
Physical activity						
No/little			**2.0**	1.2 to 3.4	**1.9**	1.1 to 3.4
Moderate			1.0		1.0	
Much			1.0	0.6 to 1.5	1.1	0.7 to 1.8
Unknown			2.5	1.0 to 6.4	**3.2**	1.3 to 8.4
Smoking						
Never			1.0		1.0	
Former			2.5	1.0 to 6.7	2.5	0.9 to 6.7
Current			**2.6**	1.0 to 6.8	**3.0**	1.1 to 7.8
Unknown			0.8	0.2 to 4.2	0.6	0.1 to 3.1
Likelihood ratio test compared with model A	p<0.01		p>0.05		p<0.005	

Values in bold are significant. Models are adjusted for all variables listed.

ascertained the appropriate identification of cancer patients within the GLOBE cohort. This makes it unlikely that the results have been biased by incompleteness of data on cancer diagnosis.

To conclude, highly educated prostate cancer patients had reduced risks of death. Although presence of comorbidities, physical activity levels and smoking status affected survival from prostate cancer, these did not explain educational inequalities in prostate survival. The role of other factors, such as capacity to obtain, process and understand health information and services, and access to healthcare, needs to be explored.

What is already known on this subject?

- Cancer survival is generally better for patients with high socioeconomic position, which has been ascribed partly to lower prevalence of other chronic diseases (comorbidities) and generally healthier lifestyle behaviours in patients with high socioeconomic position. The combined effect of comorbidities and lifestyle and cancer survival according to socioeconomic position has not been studied before.

What does this study add?

- Educational inequalities in survival were observed in prostate cancer, while no or inconsistent associations were found for breast, colon and non-small cell lung cancer. Although those with comorbidities, with no or little physical activity and current smokers had increased risk of death, these did not explain educational inequalities in prostate cancer survival.

Acknowledgements The GLOBE study is carried out by the Department of Public Health of the Erasmus University Medical Centre in Rotterdam, in collaboration with the Public Health Services of the city of Eindhoven and region Southeast Brabant. The study is supported by grants of the Ministry of Public health, Welfare and Sport and the Health Research and Development Council.

Contributors The authors made substantial contributions to this study: MJA: analysis and interpretation of data, drafting of manuscript, and critical revision of the manuscript. CBMK: acquisition of data, interpretation of data, drafting of the manuscript and critical revision of the manuscript. WJL: interpretation of data, drafting of the manuscript and critical revision of the manuscript. JWWC: interpretation of data and critical revision of the manuscript. JPM: study conception and design, acquisition of data and critical revision of the manuscript. FJL: study conception and design, acquisition of data, interpretation of data, drafting of the manuscript and critical revision of the manuscript.

Funding Name of Funder: Ministry of Public health, Welfare and Sport; Health Research and Development Council.

Competing interests None.

Ethics approval The use of personal data in the GLOBE study is in compliance with the Dutch Personal Data Protection Act and the Municipal Database Act, and has been registered with the Dutch Data Protection Authority (number 1248943).

Provenance and peer review Not commissioned; externally peer reviewed.

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