

ORIGINAL ARTICLE

Associations between education and physical functioning and pain in adult Danish cancer survivors

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ABSTRACT

Background: Late effects after cancer diagnosis and treatment are common, but only few studies have examined the role of social factors in developing these late effects. The aim of this study was to examine the association between educational level and physical function and pain among cancer survivors two years after diagnosis.

Material and methods: The study population consisted of adult Danish patients with a first-time cancer diagnosis who were sent a questionnaire in 2010 and followed up in 2012. In total, 4346 returned the first questionnaire shortly after diagnosis and 2568 returned the follow-up questionnaire. After exclusion of 177 due to missing information, we included 2391 cancer survivors in the analyses. Physical function and pain were measured using the EORTC QLQ-C30. Linear regression analyses were conducted separately for men and women, and adjusted for demographic and clinical characteristics. Additionally, analyses were stratified on comorbidity.

Results: Differences in mean scores according to educational level were small. Physical function was better in women with medium (2.8; 95% CI 0.1;5.4) and higher education (3.4; 95% CI 0.9;5.9) compared to women with short education. In contrast, men with medium education reported lower physical function (−2.9; 95% CI −5.7;−0.1) than men with short education. Compared to women with short education, we found lower pain scores among women with medium (−5.0; 95% CI −8.7;−1.4) and higher education (−3.4; 95% CI −6.7;0.0). Similarly, men with higher education experienced lower pain score (−3.4; 95% CI −6.9;0.1) than men with short education. The role of educational level differed between those with and without comorbidity.

Conclusion: Educational level is slightly associated with physical function and pain among cancer survivors. However, mean differences in this study were small and below what is considered clinically relevant.

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Reduced physical function and pain are common physical late effects following cancer treatment [1–4]. Several determinants like personal characteristics, disease, and treatment-related factors may influence the risk of developing adverse health outcomes in cancer survivors [5,6]. However, cancer and treatment-related issues are very different for the average elderly lung cancer patient and the average middle-aged breast cancer patient. In addition, the social composition of specific cancer patients differs – thus as a starting point, patients with low social position may have more both somatic and psychiatric comorbidity at time of their diagnosis [7], have more advanced stage [8–10] and thus undergo more extensive treatment with higher risk of symptoms and late effects. As a result, socially disadvantaged patients may have lower physical functioning in the survivorship phase.

Although previous studies have shown that individuals with low educational level or income have a higher incidence of lifestyle-related cancers and poorer survival compared to individuals with higher educational level or income [7,11], it

is not clear whether social position influence the development of late effects.

Chronic pain have been found to be more prevalent among women with short education compared to those with higher education in a Danish cross-sectional study of 1316 breast cancer survivors [12]. Higher education was associated with better physical function in an Italian cross-sectional study of 405 breast cancer survivors after a median of eight years since treatment [13]. Correspondingly, a Dutch cross-sectional study of 584 prostate cancer survivors 5–10 years after diagnosis showed that reduced physical function was most common among individuals with low social position (defined as economic value of the home and household income), whereas high levels of pain were most pronounced among those with intermediate social position [14].

In all, this indicates a social inequality in physical function and pain following cancer treatment. Knowledge about this would enable health professionals to identify groups with increased risk of developing these potentially severe and

debilitating late effects in order to initiate preventive efforts, early management, and treatment.

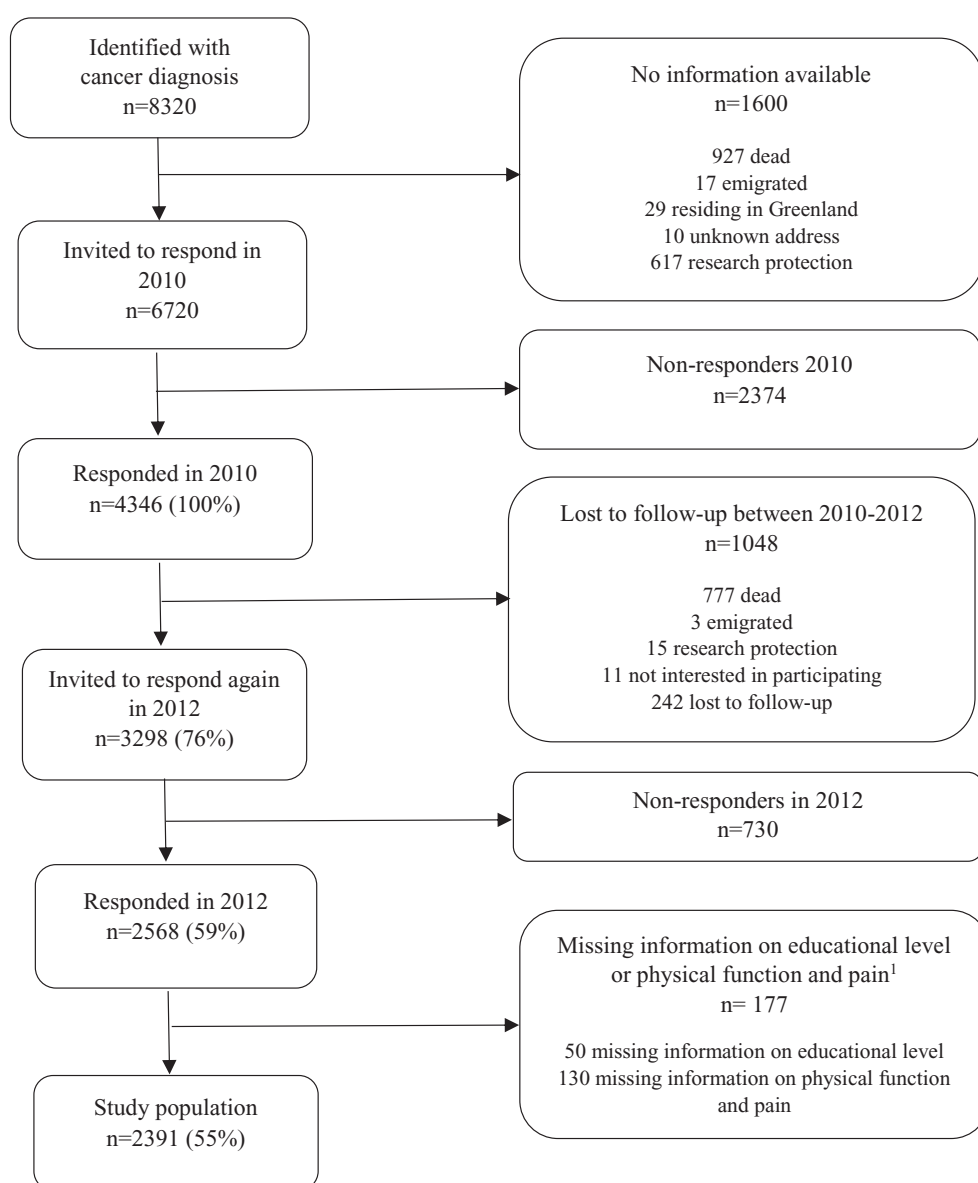
We investigated the association between social position measured as educational level and physical function and pain in adult Danish cancer survivors two years after diagnosis.

Material and methods

Study population

Data used in this study is based on two questionnaire surveys among adult cancer survivors in Denmark conducted in 2010 and 2012 by the Danish Cancer Society, which is a private, non-governmental, non-profit organization. The Danish Data Protection Agency approved both surveys (2010-41-4694). The study is described in detail elsewhere [3,15,16]. In short,

people ≥ 18 years who were diagnosed with a first-time cancer (excluding in situ and non-melanoma skin cancer) between 1 May 2010 and 31 August 2010 were identified through the Danish National Patient Registry ($N = 8320$). After exclusions due to death (11%), data protection (7%), residing in Greenland (0.4%), emigration (0.2%) and unknown address (0.1%) the remaining patients ($N = 6720$) received a questionnaire in autumn 2010 of whom 4346 people responded. A follow-up questionnaire was sent to participants who were alive approximately two years after diagnosis ($N = 3298$), and 2568 (59%) responded. Non-responders were older, more were male and unmarried, with a lower educational level, with more comorbid disorders and more often diagnosed with lung, cervix, or male genital cancers than responders. In the present study, we included information on education from the



1. Participants with missing information on educational level or missing information on both physical function, pain and loss of appetite were excluded. Three participants were categorized as missing on both exposure and outcomes.

Figure 1. Study population.

2010 questionnaire and information on physical functioning and pain from the 2012 questionnaire including 2391 cancer survivors with all available information (Figure 1).

Exposure

We used self-reported educational level as a proxy for social position. Educational level is an indicator of social position, and is a strong determinant of occupation and income. It also indicates a person's cognitive functioning and reflects receptiveness to health education and ability to cope with illness [17]. Highest attained educational level in 2010 was categorized as short education (<10 years primary or lower secondary school), medium education (10–12 years of upper secondary school or vocational education) and higher education (>12 years).

Outcome

Physical function and pain were measured in the 2012 questionnaire using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core questionnaire (EORTC QLQ-C30). EORTC QLQ-C30 is a validated questionnaire developed to measure function, symptoms, and quality of life for cancer patients [18]. It includes a measure of global quality of life, five functional scales and nine symptom scales. Physical function is based on five separate questions and pain on two questions [18]. The chosen EORTC QLQ-C30 subscales were calculated, and missing data handled in accordance with the guidelines. According to the manual, all scores were linearly transformed to a 0–100 scale, with higher scores for physical function indicating better function. Conversely, a high score on the symptom scales represents more symptoms [19]. As suggested by other authors, we used cutoff values of <66 on the functional scale and <34 on the pain scale to identify limited physical function and clinically relevant pain level corresponding to more than a little in the EORTC QLQ-C30 questionnaire [5,20].

Covariates

Information on gender, age, and cancer diagnosis was obtained from the Danish National Patient Registry. The register was established in 1977 and became compulsory in 2003 and it holds information on all admissions to both inpatient and from 1994 onwards also outpatient departments, emergency wards, and private hospitals [21]. Cancer diagnosis was categorized as breast, prostate, colorectal, smoking-related cancers, and other cancers.

Cohabitation status (married or cohabiting, widow or widowed, single) was collected in the questionnaire in 2010.

Information on surgery, radiotherapy, and chemotherapy was answered yes/no in the 2012 questionnaire. Comorbidity was also reported in the 2012 questionnaire and categorized as none, one disorder or >1 disorder including the following disorders: diabetes, heart, lung, musculoskeletal, mental, and other disorders. Furthermore, anxiety and depression scores were measured using the validated Hospital Anxiety and Depression Scale (HADS) in 2012. The questionnaire consists

of 14 items and two subscales (anxiety and depression) with scores ranging from 0 to 21 [22].

Statistical analyses

The associations between social position and scores for physical function and pain were investigated in linear regression models. Three models were applied: the first was crude unadjusted mean differences, the second model included adjustment for age, gender, and cohabitation status, and the third model included further adjustment for cancer diagnosis, surgery, radiotherapy, chemotherapy, comorbidity, anxiety, and depression score. Prior to the analyses, linearity between explanatory variables and dependent variables was inspected, and model assumptions were investigated graphically on residual plots. The analyses were stratified on gender and in a sub-analysis also on comorbidity.

p Values <5% were considered statistically significant in all analyses, and all tests were two-sided. All statistical analyses were performed using STATA 14.1 (StataCorp LP, College Station, TX).

Results

Most survivors had higher education (42%) followed by medium education (34%) and short education (24%). The most frequent diagnosis was breast cancer, and 55% of the study population were women. The mean age was 64 years and the majority was married or cohabiting (77%). Participants with short education were significantly different from participants with higher education on several characteristics. On average, women with short education were older than women with higher education ($p < 0.001$), more were widows ($p < 0.001$), had received less radiotherapy ($p = 0.04$) and chemotherapy ($p < 0.001$) and had more comorbidity ($p = 0.02$). Men with short education were older ($p < 0.001$), less had advanced cancer ($p = 0.01$) and they had higher levels of depression ($p < 0.001$) compared to men with higher education (Table 1).

Physical function

Mean scores of physical functioning by education indicated lower physical function among both men and women with short education when compared to those with higher education, although differences were small (Table 2). Among women, there was a stepwise better physical function with more education. Women with higher education reported 7.3 (95% CI 4.7;10) point higher on physical functioning compared to women with short education. In the fully adjusted model, this association was sustained but weaker (3.4 points; 0.9;5.9). Men with higher education had significantly better physical function (5.6 points; 95% CI 2.2;9.0) in the crude analyses whereas those with medium education had similar physical function compared to those with short education in crude analysis. In the fully adjusted analysis this association changed considerably with slightly worse physical function (−2.9 points; 95% CI −5.7;−0.1) among men with medium

Table 1. Short characteristics of female cancer survivors ($N = 1315$) and male cancer survivors ($N = 1076$).

	Women				<i>p</i>	Men				<i>p</i>
	Education			Education						
	Short <i>N</i> = 315	Medium <i>N</i> = 364	Higher <i>N</i> = 636	Short <i>N</i> = 257		Medium <i>N</i> = 454	Higher <i>N</i> = 365			
Age, mean years (SD)	68 (10)	62 (11)	58 (11)	<0.001 ^b	70 (9)	67 (11)	66 (11)	<0.001 ^b		
Cohabitation status, %				<0.001 ^a				0.77 ^a		
Married/cohabiting	60	76	73		83	83	85			
Widow	27	12	9		7	8	5			
Single	12	13	17		11	10	10			
Cancer diagnoses, %				0.14 ^a				0.25 ^a		
Breast	48	54	54		–	–	–			
Prostate	–	–	–		39	37	38			
Colorectal	14	13	10		21	16	16			
Smoking-related	10	6	9		21	19	20			
Other	28	28	28		20	28	27			
Advanced cancer, %				0.23 ^a				0.01 ^a		
Yes	9	13	12		21	29	32			
No	91	87	88		79	71	69			
Surgery, %				0.29 ^a				0.87 ^a		
Yes	86	90	88		62	62	64			
No	14	10	12		38	38	36			
Radiotherapy, %				0.04 ^a				0.80 ^a		
Yes	49	50	57		27	29	27			
No	51	50	43		73	71	73			
Chemotherapy, %				<0.001 ^a				0.68 ^a		
Yes	33	41	46		24	25	27			
No	67	59	54		76	75	73			
Comorbidity, %				0.02 ^a				0.37 ^a		
None	57	62	65		59	57	62			
1 disorder	26	26	26		32	29	26			
>1 disorder	17	12	9		10	14	12			
Anxiety, median (IQR)	4 (1, 7)	5 (2, 8)	4 (2, 7)	0.05 ^c	3 (1, 6)	3 (1, 6)	3 (1, 5)	0.19 ^c		
Anxiety, mean (SD)	4.7 (4.0)	5.3 (4.0)	5.1 (3.8)	0.11 ^b	4.0 (3.8)	3.9 (3.7)	3.4 (3.4)	0.11 ^b		
Depression, median (IQR)	2 (0, 5)	2 (1, 5)	2 (0, 5)	0.34 ^c	2 (0, 6)	2 (0, 5)	1 (0, 4)	<0.001 ^c		
Depression, mean (SD)	3.2 (3.4)	3.4 (3.7)	3.0 (3.2)	0.15 ^b	3.5 (3.6)	3.1 (3.5)	2.4 (3.0)	<0.001 ^b		

Some percentages do not add up to 100 because of rounding. IQR: Interquartile range; SD: standard deviation. ^a χ^2 -test; ^bANOVA test; ^cKruskal–Wallis test.

Table 2. Mean difference estimates (β) from multiple linear regression of the association between educational level and physical function and pain for women and men separately.

	Mean score	Crude Mean difference (95% CI)	Model 1 ^a Mean difference (95% CI)	Model 2 ^b Mean difference (95% CI)
Women				
Physical function		$N = 1300$	$N = 1288$	$N = 1097$
Short education	79	Ref	Ref	Ref
Medium education	82	2.7 (–0.3;5.6)	0.4 (–2.6;3.4)	2.8 (0.1;5.4)
Higher education	86	7.3 (4.7;10.0)	4.0 (1.3;6.8)	3.4 (0.9;5.9)
Pain		$N = 1288$	$N = 1278$	$N = 1097$
Short education	20	Ref	Ref	Ref
Medium education	17	–2.6 (–6.4;1.2)	–3.1 (–7.0;0.8)	–5.0 (–8.7;–1.4)
Higher education	17	–2.3 (–5.7;1.1)	–3.2 (–6.8;0.4)	–3.4 (–6.7;0.0)
Men				
Physical function		$N = 1062$	$N = 1055$	$N = 891$
Short education	82	Ref	Ref	Ref
Medium education	81	–0.7 (–4.0;2.5)	–2.5 (–5.7;0.7)	–2.9 (–5.7;–0.1)
Higher education	88	5.6 (2.2;9.0)	3.6 (0.3;7.0)	1.3 (–1.6;4.1)
Pain		$N = 1058$	$N = 1051$	$N = 888$
Short education	17	Ref	Ref	Ref
Medium education	17	–0.4 (–4.0;3.3)	0.4 (–3.4;4.1)	1.2 (–2.2;4.5)
Higher education	10	–6.9 (–10.7;–3.0)	–6.2 (–10.0;–2.3)	–3.4 (–6.9;0.1)

^aModel 1 adjusted for age and cohabitation.

^bModel 2 further adjusted for cancer diagnosis, surgery, radiotherapy, chemotherapy, comorbidity, anxiety and depression.

education than men with short education, whereas there was no significant difference between men with higher education and short education (Table 2).

Pain

In the fully adjusted models, women with medium education reported significantly lower pain scores (–5.0; 95%

CI –8.7;–1.4) compared to women with short education. No significant differences in pain were seen between women with short education and woman with higher education (Table 2). Men with higher education had lower pain scores (–6.9; 95% CI –10.7;–3.0) compared to men with short education in crude analyses. However, after adjustment the association did not reach significance (Table 2).

Table 3. Mean difference estimates (β) from multiple linear regression of the association between educational level and physical function and pain for women and men with and without comorbidity.

	Without comorbidity		With comorbidity	
	Mean difference	95% CI	Mean difference	95% CI
Women				
Physical function	N = 694		N = 403	
Short education	0	–	0	–
Medium education	3.9	(1.0;6.8)	1.1	(–4.2;6.4)
Higher education	4.2	(1.5;6.9)	2.4	(–2.6;7.4)
Pain	N = 695		N = 402	
Short education	0	–	0	–
Medium education	–4.9	(–8.7;–1.0)	–5.9	(–13.4;1.6)
Higher education	–4.8	(–8.3;–1.2)	–1.7	(–8.7;5.3)
Men				
Physical function	N = 533		N = 358	
Short education	0	–	0	–
Medium education	–3.8	(–7.1;–0.5)	–1.8	(–6.7;3.2)
Higher education	–1.4	(–4.7;2.0)	5.0	(–0.2;10.3)
Pain	N = 528		N = 360	
Short education	0	–	0	–
Medium education	2.0	(–1.7;5.8)	0.3	(–6.0;6.5)
Higher education	0.1	(–3.7;3.9)	–8.1	(–14.7;–1.4)

All estimates are adjusted for age, cohabitation, cancer diagnosis, surgery, radiotherapy, chemotherapy, comorbidity, anxiety and depression.

Stratified analysis of comorbidity

Women with medium and higher education who had no comorbid diseases had significantly better physical function [3.9 points (95% CI 1.0;6.8) and 4.2 points (95% CI 1.5;6.9), respectively] and less pain [–4.9 (95% CI –8.7;–1.0), and –4.8 points (95% CI –8.3;–1.2), respectively] compared to those with short education. This association was not present among women with comorbidity (Table 3).

No significant differences were seen between the educational groups in men without comorbidity in physical functioning or pain scores. Among men with comorbidity, those with higher education reported significantly less pain [–8.1 points (95% CI –14.7;–1.4)] compared to those with short education.

Discussion

In this cross-sectional population-based study including a large population of Danish cancer survivors, social position was associated with better physical functioning and less pain two years after diagnosis even after considering important demographic and clinical characteristics. However, mean differences in this study were small and below what is considered clinically relevant (5–10 points) [23].

As in our study, some of previous studies have shown a tendency of an association between educational level and physical function and pain among cancer survivors, although results are mixed, making it difficult to reach firm conclusions on this topic. An Italian study of 405 breast cancer survivors with a median time since treatment of eight years found that women with higher education had a slightly higher physical function compared to women with shorter education. In the same study, no association was found for 199 survivors of colon cancer after a median of five years after diagnosis [13]. In line with this, no associations between education and

physical functioning or pain was found after adjustment for clinical variables, lifestyle factors, comorbidity, and cohabitation among 369 Danish head and neck cancer survivors [5]. Findings of three Nordic cross-sectional studies of pain among breast cancer survivors ($N=116$, 832 and 2000) approached between two and 17 years after diagnosis, pointed in different directions. In Sweden, no association was found between educational level and pain [1]. In Denmark, Peuckmann et al. found higher levels of pain among women with short and medium education compared to those with higher education [12]. In contrast, Norwegian women with medium and higher education reported more pain than those with short education [2].

Limited physical functioning and pain are debilitating late effects that may negatively affect the quality of life of survivors. The fact that we only found moderate differences in physical function and pain according to educational level could reflect reality. These results could though also be due to methodological issues.

Educational level is a robust proxy for social position, relatively stable throughout adult life and straightforward to self-report in a questionnaire [17]. Other indicators of social position such as income or occupation may change several times during life and especially in connection with illness, thus would require several measurements to ensure a reliable categorization during the period of up to 2½ years after cancer diagnosis the present study covers. Using education introduce a risk of misclassification among older patients due to a different pattern of education across birth cohorts.

Self-reported physical function and symptoms of pain captures the individual experience, and we find no reason to believe that this reporting is biased. The EORTC QLQ-C30 questionnaire was developed to detect acute symptoms of cancer treatment; however, it is commonly used in late effect studies due to a lack of a specific questionnaire. In general, one may expect a social inequality in both physical function and symptoms like pain due to social differences in life style, work, and other environmental exposures [24]. Therefore, the most important limitation of the present study is the lack of precancer physical function and pain as it made us unable to separate preexisting physical function and pain symptoms from those induced by cancer diagnosis and treatments.

Cancer patients were identified through the Danish National Patient Register, which ensured a close to complete nationwide identification [21]. However, responders to the two surveys who the present study is based on had higher educational level, less comorbidity, and overall a better prognosis compared to non-responders. It is reasonable to assume that those who did not respond to the questionnaire were possibly those with the worse health and highest risk of physical late effects independent of socioeconomic group [25]. The high scores in physical function and low scores in pain compared to scores from the general Danish population [26] further support that our sample consisted of the best functioning cancer survivors, which may have contributed to limited variance and hence the small differences observed in physical late effects between the educational groups.

Age, comorbidity and treatment with chemotherapy were confounding factors in the association between educational

level and physical function and pain as illustrated in the multivariate modeling. Information on other risk factors such as smoking and overweight that may affect physical function and pain were not available. Furthermore, adjustment for participation in rehabilitation would have strengthened the study, as we know that this is more common among higher educated [27].

Conclusion

In this large population-based study of Danish cancer survivors, women have slightly better physical function and less pain with increasing educational level. Men with higher education reported less pain and those with medium education have worse physical function compared to men with short education. The role of educational level seems to differ slightly between those with and without comorbidity.

Educational level may be a risk factor to take into account when assessing the need for rehabilitation among cancer survivors. Further studies investigating the association between educational level and physical late effects taking precancer functional level and symptoms into account are needed in larger samples of survivors with specific cancer diagnosis.

Disclosure statement

No potential conflict of interest was reported by the authors.

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