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Who are the cancer survivors? A nationwide study in Denmark, 1943–2010

H B Hovaldt*[,1,2], N P Suppli[1], M H Olsen[1], M Steding-Jessen[3], D G Hansen[4], H Møller[5], C Johansen[1,6] and S O Dalton[1]

[1]Danish Cancer Society Research Center, Unit of Survivorship, Strandboulevarden 49, DK-2100 Copenhagen Ø, Denmark; [2]Department of Psychology, University of Copenhagen, Øster Farimagsgade 2a, DK-1353 Copenhagen K, Denmark; [3]Danish Cancer Society, Documentation and Quality, Strandboulevarden 49, DK-2100 Copenhagen Ø, Denmark; [4]National Research Center for Cancer Rehabilitation, Research Unit of General Practice, University of Southern Denmark, J.B. Winsløws Vej 9, Entrance B, 1st Floor, DK-5000 Odense C, Denmark; [5]King's College London, Section of Cancer Epidemiology and Population Health, Bermondsey Wing, 3rd Floor, Guy's Hospital, Great Maze Pond, London SE1 9RT, UK and [6]Department of Oncology, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen Ø, Denmark

Background: No nationwide studies on social position and prevalence of comorbidity among cancer survivors exist.

Methods: We performed a nationwide prevalence study defining persons diagnosed with cancer 1943–2010 and alive on the census date 1 January 2011 as cancer survivors. Comorbidity was compared by social position with the non-cancer population.

Results: Cancer survivors composed 4% of the Danish population. Somatic comorbidity was more likely among survivors (OR 1.59, 95% CI 1.57–1.60) and associated with higher age, male sex, short education, and living alone among survivors.

Conclusions: Among cancer survivors, comorbidity is common and highly associated with social position.

The number of cancer survivors is increasing in many countries (Engholm *et al*, 2010; Maddams *et al*, 2012; de Moor *et al*, 2013), mainly due to ageing populations and decreasing cancer mortality as a result of better diagnostics and treatment (Moller *et al*, 2002; Jemal *et al*, 2004; Australian Institute of Health and Welfare, Cancer Australia & Australasian Association of Cancer Registries, 2008; Rowland and Bellizzi, 2008; Parry *et al*, 2011). To our knowledge, no nationwide studies of social position and the prevalence of comorbidity have been performed among cancer survivors. Defining cancer survivors from date of diagnosis and throughout their lives (National Cancer Institute, 2014), we thoroughly characterised the national population of such survivors, compared the total burden of severe somatic comorbidity in cancer survivors and the non-cancer population, and described potential differences by social position among the cancer survivors.

MATERIAL AND METHODS

Study design and population. We performed a cross-sectional study of all people living in Denmark on 1 January 2011, who were identified in the civil registration system, comprising 5 560 628 people (Pedersen, 2011). Since 1943, all cases of cancer have been registered in the Danish Cancer Registry (Gjerstorff, 2011). We identified all persons diagnosed with cancer (excluding benign tumours, *in situ* cancers and non-melanoma skin cancers) in 1943–2010 and classified them according to their first (index) cancer.

Somatic comorbidity measured by the Charlson Comorbidity Index (CCI) was calculated based on discharge information from 1978 (inpatient) and 1995 (outpatient) to census date from the National Patient Registry (Lynge *et al*, 2011) and information on all subsequent primary malignancies after the index cancer from the Danish Cancer Registry (Charlson *et al*, 1987; Dalton *et al*, 2008a). From the Danish Psychiatric Case Register (Mors *et al*, 2011), we defined severe psychiatric comorbidity as hospital contacts from 1969 (inpatient) or 1995 (outpatient) to the census date for schizophrenia and psychosis and affective disorders (Dalton *et al*, 2008a).

Education and cohabitation status was used as indicators for social position. Information was derived from the Integrated Database for Labour Market Research in Statistics Denmark (Thygesen, 1995) and the Danish Civil Registration System

*Correspondence: HB Hovaldt; E-mail: habiho@cancer.dk or hanna.hovaldt@psy.ku.dk

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containing information on all Danish residents. Social position analyses were restricted to 30–90-year olds, as information on education was not available for people born before 1920, and many Danes finish their education in the late twenties. Highest attained educational level was categorised as short (mandatory education, 7–9 years), medium, (high school or vocational education, 8–12 and 10–12 years of education for people born before and after 1958, respectively), and long education (>12 years, i.e., higher education). Cohabitation status was defined as cohabiting (married or cohabiting with partner), widow/widower, divorced, and single (not cohabiting and never married).

Statistical analysis. The prevalence of cancer survivors was calculated from the number of people with a cancer diagnosis in the population on 1 January 2011. To analyse the risk for a CCI score ⩾1 depending on being a cancer survivor, multivariate logistic regression analyses were performed with adjustment for sex, age, schizophrenia or psychosis, and affective disorders. The association between education and cohabitation status and somatic comorbidity was examined in 30–90-year olds by multivariate logistic regression analyses stratified by cancer survivor or non-cancer population and time since diagnosis and adjusted for education, cohabitation status, sex, age, schizophrenia or psychosis, affective disorder, and cancer diagnosis (only in cancer survivors). Age was modelled as a second-order polynomial in all regression analyses.

RESULTS

On 1 January 2011, 227 704 cancer survivors were living in Denmark, corresponding to 4% of the total population. The median age of the cancer survivors was 67 years; 13% of 60–89-year olds and 18% of ⩾90-year olds were cancer survivors (Table 1). Nearly 8% of cancer survivors had had more than one cancer (Table 2).

Median time since diagnosis was 6 years. Approximately one-third of people with cancers of the lung, esophagus, stomach, and pancreas had survived <1 year after diagnosis. One-third of survivors of female genital cancers had received their diagnosis ⩾20 years before the census date, but only 4% of lung cancer survivors (Supplementary Information S1).

A CCI score ⩾1 was found for 40% of the cancer survivors and for 16% of the non-cancer population, whereas prevalence of affective disorders and schizophrenia or psychosis was similar

Table 1. Basic characteristics of 5 560 628 people living in Denmark on 1 January 2011

	Cancer survivors			Non-cancer population			
	Total, $n=227\,704$	Men, $n=94\,481$	Women, $n=133\,223$	Total, $n=5\,332\,924$	Men, $n=2\,662\,101$	Women, $n=2\,670\,823$	Proportion cancer survivors[e]
	%[a]	%[a]	%[a]	%[a]	%[a]	%[a]	%
Age on 1 January 2011 (years)							
0–29	2	3	1	37	38	37	<1
30–59	26	24	27	42	52	41	3
60–89	69	72	67	21	20	22	13
⩾90	3	2	4	1	<1	1	18
Charlson Comorbidity Index							
0	60	56	63	85	84	85	3
1	19	20	18	11	11	10	7
⩾2	21	25	19	5	5	4	17
Schizophrenia or psychosis							
Ever diagnosed	1	1	1	1	1	1	4
Never diagnosed	99	99	99	99	99	99	4
Affective disorder							
Ever diagnosed	4	3	5	3	2	3	6
Never diagnosed	96	97	95	97	98	97	4
	Total[b], $n=218\,003$	Men[b], $n=90\,789$	Women[b], $n=127\,214$	Total[b], $n=3\,313\,351$	Men[b], $n=1\,637\,833$	Women[b], $n=1\,675\,518$	
	%[a]	%[a]	%[a]	%[a]	%[a]	%[a]	%
Education[c]							
Short	26	24	28	16	15	17	10
Medium	49	51	47	52	55	50	6
Long	23	23	23	28	26	31	5
Cohabitation status							
Cohabiting	65	75	58	71	74	69	6
Widow/widower	18	9	24	7	3	11	15
Divorcee	11	8	12	9	8	11	7
Single[d]	7	8	6	13	15	10	3

[a]The sum may exceed 100% due to rounding.
[b]Restricted to 30–90-year olds.
[c]Excluding unknown education: 2% of cancer survivors, 3% of non-cancer population.
[d]Not cohabiting and never married.
[e]The proportion, who are cancer survivors of the total number of people in each category.

(Table 1). The proportion of survivors with a CCI score ⩾1 ranged from 58% for lung cancer survivors to 29% for survivors of malignant melanoma. In comparison with the non-cancer population, the OR of all cancer survivors for having a CCI score ⩾1 was 1.59 (95% CI 1.57–1.60) after adjustment for sex and age. Adjustments for psychiatric comorbidity did not change the estimate. Male sex and older age were associated with significantly increased odds for a CCI score ⩾1 (data not shown).

Level of education and cohabitation status varied by cancer type, but cancer survivors with short education had the highest proportion of somatic and psychiatric comorbidity in all the age groups (Supplementary Information S2). Compared with survivors with higher education, those with short education had 57% higher odds for having a CCI score ⩾1 (95% CI 1.53–1.62), and survivors with medium education had 33% higher odds (95% CI 1.29–1.36). Living alone was also significantly associated with higher odds for a CCI score ⩾1 in comparison with cohabiting; divorced people had the highest odds (OR 1.45, 95% CI 1.41–1.50) (Table 3). The social gradient in somatic comorbidity was slightly smaller among cancer survivors than the non-cancer population and tended to be smaller with time after diagnosis (Table 3).

Table 2. Cancer-specific characteristics of 227 704 cancer survivors living in Denmark on 1 January 2011

	Total, $n = 227\,704$, %[a]	Men, $n = 94\,481$, %[a]	Women $n = 133\,223$, %[a]
Index cancer type[b]			
Mouth, pharynx and larynx	2	4	1
Esophagus, stomach and pancreas	1	2	1
Colon and rectum	11	13	10
Lung	3	3	3
Breast	23	<1	39
Female genitalia	10	-	17
Male genitalia	13	32	-
Kidney and bladder	8	14	4
Malignant melanoma	8	8	9
Central nervous system	6	6	6
Leukemias, NHL and HL	7	9	5
Other cancers	7	8	6
Age at diagnosis of index cancer (years)			
0–29	6	8	6
30–59	46	35	51
60–89	48	56	42
⩾90	<1	<1	1
Time since diagnosis of index cancer (years)			
<1	11	13	9
1–4	31	36	27
5–9	22	22	22
10–19	22	18	25
⩾20	15	11	18
No. of primary cancers after index cancer[b]			
0	93	93	93
1	7	7	7
⩾2	1	1	1

Abbreviations: HL = Hodgkin lymphoma; NHL = non-Hodgkin lymphoma.
[a]The sum may exceed 100% due to rounding.
[b]Excluding benign tumours, cancer *in situ*, and non-melanoma skin cancers.

DISCUSSION

Cancer survivors have substantially higher odds for comorbid diseases in addition to their cancer than the cancer-free population. Short education and living alone were consistently associated with higher odds for comorbid diseases.

Our results confirm the prevalence of cancer type, age, sex and time since diagnosis found previously (Maddams *et al*, 2009; Siegel *et al*, 2012; Underwood *et al*, 2012; de Moor *et al*, 2013; Gatta *et al*, 2013; Jarlbaek *et al*, 2014); however, this is the first study to report results from a nationwide population with combined registry-based information on both cancer, demography, comorbidity, and social position.

Results from the National Health Interview Survey in the United States ($n = 7292$) indicated a higher prevalence of somatic comorbidity among both cancer survivors (57.7%) and matched controls (45.2%) than in our study; however, the survey data on comorbidity were self-reported in relation to functional limitations (Yabroff *et al*, 2004). We ensured consistent reporting of severe comorbid diseases leading to hospital contacts and found that cancer survivors had significantly greater odds for somatic comorbidity than the non-cancer population, which might be due to preexisting morbidity, late effects of cancer and cancer treatment, shared risk factors such as lifestyle, environmental exposure, and genetics, or joint effects of these (Aziz, 2007). Furthermore, the non-cancer illness of cancer survivors may not be

Table 3. Multivariate logistic regression analyses of the odds ratio (OR) with 95% confidence intervals (95% CIs) between somatic comorbidity (CCI ⩾1), education, and cohabitation status among cancer survivors ($n = 218\,003$) and the non-cancer population ($n = 3\,313\,351$) aged 30–90 years, living in Denmark on 1 January 2011, adjusted for sex and age

	Non-cancer population, $n = 3\,313\,351$		Cancer survivors, $n = 218\,003$		Cancer survivors <1 year after diagnosis, $n = 23\,958$		Cancer survivors 1–4 years after diagnosis, $n = 67\,262$		Cancer survivors 5–9 years after diagnosis, $n = 47\,577$		Cancer survivors 10–19 years after diagnosis, $n = 47\,539$		Cancer survivors ⩾20 years after diagnosis, $n = 31\,667$	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Education														
Short	1.71	1.70–1.73	1.57	1.53–1.62	1.74	1.60–1.89	1.64	1.56–1.72	1.63	1.53–1.72	1.49	1.41–1.58	1.40	1.31–1.51
Medium	1.34	1.33–1.35	1.33	1.29–1.36	1.39	1.29–1.49	1.35	1.29–1.40	1.34	1.27–1.41	1.31	1.25–1.38	1.24	1.17–1.32
Long	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
Cohabitation status														
Cohabiting	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
Widow/widower	1.11	1.10–1.13	1.14	1.11–1.17	1.17	1.07–1.27	1.18	1.12–1.24	1.12	1.06–1.18	1.11	1.05–1.18	1.11	1.04–1.18
Divorced	1.48	1.47–1.50	1.45	1.41–1.50	1.52	1.40–1.66	1.46	1.38–1.54	1.49	1.40–1.59	1.43	1.35–1.53	1.33	1.24–1.44
Single[a]	1.24	1.23–1.26	1.25	1.21–1.30	1.23	1.10–1.38	1.29	1.20–1.38	1.26	1.16–1.37	1.19	1.10–1.29	1.21	1.10–1.33

Abbreviation: CCI = Charlson Comorbidity Index.
[a]Not cohabiting and never married.

managed optimally (Earle and Neville, 2004) contributing to the risk of hospitalisation for comorbidity.

Previous studies have shown that low social position is associated with higher cancer incidence for selected cancers and poorer survival after most cancers (Dalton *et al*, 2008b) and a higher risk for comorbid disease at the time of cancer diagnosis (Louwman *et al*, 2010). We show that the social gradient continues into life after cancer, a gradient that could not be explained by case-mix due to cancer type alone. We found that the social differences were smaller among those who had survived longer, which might be due to the social gradient in cancer survival (Dalton *et al*, 2008b), and because comorbidity is a strong predictor for early mortality from cancer (Yancik *et al*, 2001; Piccirillo *et al*, 2004).

The primary aim of this study was to characterise comorbidity and social position in a nationwide population of cancer survivors; however, information on individual lifestyle and behaviour could have provided further insight, as these are risk factors for both cancer and comorbid diseases. As the aim was to investigate the total burden of severe comorbidity, we included all comorbid diseases occurring before and after the index cancer. As secondary primary malignancies were included only for cancer survivors, comorbidity might be a late effect of cancer treatment and/or due to shared risk factors. Most comorbid conditions in people with recent cancers date from before the index cancer, while people with earlier cancers have comorbid conditions from after the index cancer. Finally, time since diagnosis was truncated, as cancer registration started in 1943; thus, people with cancers diagnosed before 1943, and alive on 1 January 2011, were not defined as cancer survivors but we expect the underestimation of prevalence to be small.

This study, based on nationwide data, provides new insight into the total burden of severe comorbidity in the growing group of cancer survivors. Use of national registers prevents bias and provides consistent, complete, and valid individual-level information on social factors and morbidity, and the long tradition of systematic registration of cancer in Denmark ensures almost complete registration of cases.

CONCLUSION AND IMPLICATIONS

The population of Danish cancer survivors is large and some have survived for decades after their initial diagnosis. Beyond being impaired by the cancer treatment, cancer survivors are more affected by other chronic disorders than their non-cancer fellows, especially survivors with low social position. Further investigation of the causes of social differences in comorbidity are important to ensure equal access and optimal care and rehabilitation of both cancer and comorbid diseases for all cancer survivors.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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