Published OnlineFirst October 20, 2020; DOI: 10.1158/1055-9965.EPI-20-0721

Social Inequalities in Cancer Survival in Belgium: A Population-Based Cohort Study

Michael Rosskamp[1], Julie Verbeeck[1], Victoria Sass[2,3], Sylvie Gadeyne[2], Freija Verdoodt[1], and Harlinde De Schutter[1]

ABSTRACT

Background: Socioeconomic status (SES) is an important factor in cancer survival; however, results are heterogeneous and linked to characteristics of the study population and health care system. This population-based cohort study evaluates the association between individual-level socioeconomic and demographic factors and cancer survival for the first time in Belgium.

Methods: From the Belgian Cancer Registry, we identified 109,591 patients diagnosed between 2006 and 2013 with one of eight common cancer types. Information on treatment, socioeconomic parameters, and vital status were retrieved from multiple data sources and linked using a unique personal identification number. The outcome was 5-year observed survival. Associations between survival and socioeconomic and demographic factors were assessed using multivariable Cox proportional–hazard regression models.

Results: Lower income, unemployment, and living alone were all associated with worse cancer survival. These associations were most pronounced for certain lifestyle-related cancer types (e.g., head and neck cancers) and those with good to moderate prognosis (e.g., colorectal and female breast cancer).

Conclusions: These results indicate that, despite a comprehensive and nationwide health insurance program in which equity in rights and access to health care are pursued, SES is associated with disparities in cancer survival in Belgium.

Impact: This population-based study with individual-level socioeconomic information of more than 100,000 patients with cancer identifies patient groups that may be at highest risk for socioeconomic disparities in cancer survival. Reasons behind the observed disparities are multiple and complex and should be further examined. Health policy interventions should consider the observed deprivation gap to plan targeted actions.

Introduction

Overall, socioeconomic status (SES) is associated with inequalities in healthcare usage, morbidity, and mortality. Cancer is no exception. Numerous studies have shown an association between socioeconomic (SE) and sociodemographic (SD) factors and cancer risk, cancer mortality, and cancer survival. However, these associations are not homogeneous across regions and ethnical groups, nor across cancer types (1). The effects on risk and prognosis are heterogeneous and not yet fully understood (2, 3).

As for cancer survival, a poorer prognosis for lower SE groups has consistently been observed. Despite a global improvement in cancer survival, mainly through advancements in diagnostics and treatments, the gap between deprived and affluent patients has increased over time (4–6).

In Belgium so far, most studies focused on the impact of SE and SD factors on cancer mortality (7–9). Although crucial for public health and healthcare policies, mortality rates depend on both the risk of and survival from a disease. In addition, mortality rates are subject to the accuracy of death certification, which can be challenging, especially in older patients representing a large proportion of cancer cases (10). In this study, we will therefore focus on the association between SES and survival among patients with cancer.

SES is a complex, multifaceted concept consisting of several dimensions (11). So far, numerous studies concerning cancer-related outcomes operationalized SES either by a single variable (often income as a proxy for material wealth, educational attainment reflecting chances in early life, or unemployment rate as a proxy for area-deprivation; ref. 12), or by a composite deprivation index to group patients into SE groups (13). Although strongly related, different SE and SD factors tap into different causal pathways on how SES influences the onset and course of diseases, highlighting the importance of considering multiple SE and SD indicators separately.

The objective of this population-based cohort study is to assess, for the first time in Belgium, the association between cancer survival and different dimensions of SES, more specifically, household income, employment, and marital status. Second, this study also aims to explore if observed associations can be (partly) explained by specific clinical characteristics such as tumor characteristics, stage at diagnosis, comorbid conditions, and detailed primary treatment information.

Materials and Methods

Patient selection and data sources

Data were retrieved from three databases and linked through a unique personal identification number assigned to all residents of Belgium (1:1 linkage): the Belgian Cancer Registry, the Crossroads Bank for Social Security (CBSS), and the reimbursement databases of the health insurance companies gathered by the Intermutualistic Agency (IMA).

Patients diagnosed with cancer between 2006 and 2013, ages 25 years and older at time of diagnosis and registered in the IMA database were

[1]Belgian Cancer Registry, Brussels, Belgium. [2]Department of Sociology, Interface Demography, Vrije Universiteit Brussel, Brussels, Belgium. [3]Department of Sociology, University of Washington, Seattle, Washington.

Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

Corresponding Author: Harlinde De Schutter, Belgian Cancer Registry, Rue Royale 215, Brussels 1210, Belgium. Phone: 32-2-250-1010; Fax: 32-2-250-1011; E-mail: harlinde.deschutter@kankerregister.org

Cancer Epidemiol Biomarkers Prev 2020;XX:XX–XX

doi: 10.1158/1055-9965.EPI-20-0721

Published OnlineFirst October 20, 2020; DOI: 10.1158/1055-9965.EPI-20-0721

identified using the Belgian Cancer Registry, a nationwide register that holds information on all primary invasive cancer diagnoses since 2004 (14). Using the 10th International Classification of Diseases (ICD-10), eight cancer types were included in this study: Colon (C18–19), rectal (C20), female breast (C50), lung (C34), ovarian (C56), head and neck (C00-C14,C30-C32), pancreatic (C25) and stomach (C16.1-C16.9) cancer. These sites were selected because they represent high-burden cancers for which treatment data were reliably available. For each of these cancer types, a random sample (2/3 if less than 10,000 cases present in the registry, otherwise 1/2) was drawn from the total patient population and included in the study. Stratified sampling was performed by age quartiles (for each cancer type) and sex (if applicable). Single random sampling was applied using the PROC SURVEYSELECT procedure in SAS 9.3 (SAS Institute Inc.). From the Belgian Cancer Registry, we extracted information on patient (age and sex) and tumor (stage and subtype) characteristics. For head and neck cancer and stomach cancer, subtypes were defined on the basis of the primary tumor topography. Histological subtypes were considered for female breast cancer, as well as lung, ovarian, and pancreatic cancer. Topography and morphology codes are available in Supplementary Table S1. A combined TNM stage, where the pathological stage prevails over the clinical, except for cases diagnosed with clinical stage IV (i.e., category cM1 for most cases), was considered (14).

From the reimbursement databases of the health insurance companies, covering 97% of the Belgian population, we extracted detailed information on primary tumor-directed treatment schemes [i.e., charged nomenclature codes for surgery and radiotherapy, and Anatomical Therapeutic Chemical (ATC; ref. 15) codes for chemotherapy], and data on comorbidities (chronic respiratory and cardiovascular comorbidities and diabetes mellitus) treated before cancer diagnosis (16). As IMA data do not directly refer to a specific diagnosis, timeframes around the cancer diagnosis were used to assess primary cancer treatment: surgery was included if undergone within one month before until 6 months after diagnosis, chemo- and radiotherapy were included if administered within one month before diagnosis until 6 months after diagnosis or surgery (if applicable; ref. 17).

Vital status information was extracted from CBSS. SE and SD data were extracted from the same database, including household income, employment, and marital status. The CBSS integrates socioeconomic data from several Belgian social security institutions and public entities, for research and administrative purposes. The majority of data are registered on a quarterly basis for all inhabitants of Belgium (18).

To avoid the impact of cancer on the patient's SE status, the retrieved data referred to the patient's situation in the year before diagnosis (trimester of cancer diagnosis excluded). Income was available at the household level by increments of 5,000€. Weights were calculated for each household based on its composition: 1.0 to the first adult; 0.5 to the second and each subsequent person ages 12 years and over; 0.3 to each child under 12 years of age. The household income was then divided by the sum of the weightings (equivalized) to yield a representative income, according to the OECD-modified scale (19). Low-, middle-, and high-income households were defined using cutoffs at p25 and p50 and considering the active (patients younger than 65 years and non-retired) and non-active (ages 65+ years or retired) cancer population separately (20). Employment status among (potentially) active patients was classified as employed, unemployed and job-seeking, and unemployed and not job-seeking. The latter category consisted of people who could not work due to incapacity/disability or due to other reasons (8).

De jure marital status was divided into the following categories: Living together, separated, single and widowed, and was available for the period 2009–2013 only.

Follow-up and outcome analyses

The start of follow-up for each patient was the date of cancer diagnosis. Vital status information was available until July 1, 2016. The outcome was observed survival during the 5-years after diagnosis. Patients whose observation duration was shorter than the maximum time for which survival probability was calculated (e.g., some patients had an early diagnosis but were lost to follow-up because they were no longer found at CBSS; $n = 175$) were censored at the date of last information on vital status (21).

Depending on the SE or SD factor, analyses were performed considering the whole-study cohort (marital status), the (potentially) active population (household income and employment status) or the non-active population (household income). Because of the different nature of household income in the active and non-active population (i.e., salary and pension, respectively), analyses were performed separately.

Following univariable analyses, the relationships between survival and household income, employment, and marital status were assessed using multivariable Cox proportional-hazards regression models, adjusting for age (continuous), gender (if applicable, binary), tumor subtype (except for colon and rectal cancer, categorical), stage at diagnosis (categorical), chronic cardiovascular disease (binary), chronic respiratory disease (binary), diabetes mellitus (binary), and primary treatment scheme (at baseline, categorical). Cases with unknown stage were included in the study and considered as a distinct category. Furthermore, cases with non-specified or less-common subtypes were combined into a separate category.

Results were presented as hazard ratios (HR) with 95% confidence intervals (95% CI). To fulfil proportional hazard assumptions, interactions with time-points and two-way interactions for variables with significant effects in the model were considered under the threshold of alpha = 0.01 using a backward interaction selection procedure (22).

Sensitivity analyses

First, the association between 5-year observed survival and individual, household and neighborhood-level income was assessed in uni- and multivariable Cox proportional–hazards regression models. Second, to assess the potential mediator effect of stage at diagnosis and comorbid conditions, adjusted survival estimates were calculated without considering those adjustment factors. Likewise, the effect of treatment on survival estimates was assessed by removing this adjustment factor from the multivariable regression models.

All analyses were conducted in SAS 9.3 (SAS Institute Inc.).

Results

Descriptive analysis

Patient and tumor characteristics by cancer type are shown in **Table 1**. A total of 109,591 patients (female breast, $n = 33,644$; colon, $n = 20,149$; rectum, $n = 8,174$; head and neck, $n = 7,304$; lung, $n = 27,668$; ovary, $n = 3,394$; pancreas, $n = 4,737$; stomach, $n = 4,521$) with a median follow-up time of 3.0 years (interquartile range, 0.9–5.0 years) were included. Of these, 60,206 patients (54.9%) were women and 38,168 of all patients (34.8%) were younger than 65 years old and non-retired at time of diagnosis. The percentage of patients treated for chronic respiratory and cardiovascular comorbidities or diabetes

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Table 1. Patient and tumor characteristics by cancer type, Belgium 2006–2013.

	Breast cancer (n = 33,644)	Lung cancer (n = 27,668)	Colon cancer (n = 20,149)	Rectal cancer (n = 8,174)	Head and neck cancers (n = 7,304)	Pancreatic cancer (n = 4,737)	Stomach cancer (n = 4,521)	Ovarian cancer (n = 3,394)
Patient characteristics	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**
Gender								
Male	—	20,907 (75.6)	11,567 (57.4)	5,283 (64.6)	5,871 (80.4)	2,648 (55.9)	3,109 (68.8)	—
Female	33,644 (100.0)	6,761 (24.4)	8,582 (42.6)	2,891 (35.4)	1,433 (19.6)	2,089 (44.1)	1,412 (31.2)	3,394 (100.0)
Age and professional status at diagnosis								
<65 years and nonretired (active)	17,243 (51.3)	7,714 (27.9)	3,989 (19.8)	2,208 (27.0)	3,565 (48.8)	1,152 (34.3)	1,017 (22.5)	1,280 (37.7)
65+ years or retired (nonactive)	16,401 (48.8)	19,954 (72.1)	16,160 (80.2)	5,966 (73.0)	3,739 (51.2)	3,585 (75.7)	3,504 (77.5)	2,114 (62.3)
Mean age (standard deviation)	*61.7 (14.3)*	*68.7 (10.7)*	*72.1 (12.0)*	*69.5 (12.1)*	*63.1 (10.8)*	*70.0 (11.7)*	*71.5 (12.8)*	*66.1 (14.1)*
Comorbidity[a]								
Chronic respiratory	1,054 (3.1)	4,635 (16.8)	1,137 (5.6)	470 (5.8)	631 (8.6)	257 (5.4)	277 (6.1)	122 (3.6)
Chronic cardiovascular	12,787 (38.0)	15,375 (55.6)	11,473 (56.9)	4,183 (51.2)	3,229 (44.2)	2,765 (58.4)	2,552 (56.5)	1,511 (44.5)
Diabetes mellitus	2,982 (8.9)	3,799 (13.3)	3,189 (15.8)	1,162 (14.2)	727 (10.0)	1,277 (27.0)	757 (16.7)	351 (10.3)
Tumor characteristics	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**
Subtype[b]								
	IDC 25,410 (75.5)	ADC 10,717 (38.7)	—	—	HP 904 (12.4)	ADC 3,689 (77.9)	GOJ 1,353 (29.9)	ADC 2,638 (77.7)
	ILC 4,426 (13.2)	LCLC 1,169 (4.2)	—	—	LX 2,285 (31.3)	PNET 332 (7.0)	GB 1,338 (26.6)	Other 756 (22.3)
	Other 3,808 (11.3)	SCLC 4,132 (14.9)	—	—	OC 2,055 (28.1)	Other 716 (15.1)	Other 1,830 (40.5)	
		SCC 7,602 (27.5)			OP 2,060 (28.2)			
		Other 4,048 (14.6)						
Combined stage								
I	13,782 (41.0)	4,309 (15.6)	3,151 (15.6)	2,046 (25.0)	1,322 (18.1)	385 (8.1)	868 (19.2)	610 (18.0)
II	11,791 (35.1)	1,943 (7.0)	6,115 (30.4)	1,797 (22.0)	870 (11.9)	1,065 (22.5)	669 (14.8)	196 (5.8)
III	4,092 (12.2)	5,421 (19.6)	5,167 (25.6)	2,136 (26.1)	1,018 (13.9)	359 (7.6)	772 (17.1)	961 (28.3)
IV	1,878 (5.6)	10,318 (37.3)	3,800 (18.9)	1,329 (16.3)	2,971 (40.7)	1,786 (37.7)	1,157 (25.6)	660 (19.5)
X (unknown)	2,101 (6.2)	5,677 (20.5)	1,916 (9.5)	866 (10.6)	1,123 (15.4)	1,142 (24.1)	1,055 (23.3)	967 (28.5)
Primary treatment scheme								
Surgery only	902 (2.7)	5,017 (18.1)	10,014 (49.7)	2,338 (28.6)	1,340 (18.4)	514 (10.9)	1,240 (27.4)	512 (15.1)
Surgery + (neo-)adjuvant	27,800 (82.6)	6,009 (21.7)	7,539 (37.4)	4,406 (53.9)	1,465 (20.1)	674 (14.2)	884 (19.6)	1,791 (52.8)
Chemo ± RT ± HT	4,110 (12.2)	10,216 (36.9)	1,335 (6.6)	768 (9.4)	4,016 (55.0)	2,140 (45.2)	1,046 (23.1)	737 (21.7)
No tumor-directed treatment	832 (2.5)	6,426 (23.2)	1,261 (6.3)	662 (8.1)	483 (6.6)	1,409 (29.7)	1,351 (29.9)	354 (10.4)

Abbreviations: ADC, adenocarcinoma; GB, gastric body; GOJ, gastro–esophageal junction; HP, hypopharynx; HT, hormonal therapy (only considered for breast cancer); IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; LCLC, large-cell lung cancer; LX, larynx; OC, oral cavity; OP, oropharynx; PNET, primitive neuro-ectodermal tumor; RT, radiotherapy; SCC, squamous cell carcinoma; SCLC, small-cell lung cancer.

[a]Comorbidity data were extracted from the administrative databases of the health insurance companies and referred to patients treated before cancer diagnosis.

[b]Subtypes are based on morphology codes, except for head and neck cancers and stomach cancer for which topography codes were considered.

[c]Combined stage: The pathological stage prevails over the clinical, except for cases diagnosed with clinical stage IV.

Published OnlineFirst October 20, 2020; DOI: 10.1158/1055-9965.EPI-20-0721

mellitus before the cancer diagnosis were 7.8%, 49.2%, and 13.0%, respectively. Furthermore, 59,715 patients (54.5%) died within 5 years after diagnosis. This percentage varied largely by cancer type: From 21.8% for breast cancer to 90.3% for patients with pancreas cancer.

Male predominance was most pronounced in head and neck (80.4%) and lung cancer (75.6%). Mean age at diagnosis differed strongly by cancer type, with female breast cancer (51.3%) and head and neck cancers (48.8%) being most often diagnosed in the (potentially) active population, whereas colon cancer affected mostly the older, non-active population (80.2%). The percentage of patients with chronic respiratory comorbidity was highest in the lung cancer cohort (16.8%), whereas cardiovascular comorbidities were present in almost half of the patients across the different cancer types, except breast cancer. Diabetes was largely associated with age, resulting in higher proportions for patients with colon (15.8%), pancreatic (27.0%), and stomach cancer (16.7%). Stage distribution varied across cancer types; whereas the majority of breast cancer cases were diagnosed at an early stage, more than one third of lung, pancreas, and head and neck cancers were diagnosed at stage IV of the disease. Missing information on stage at diagnosis ranged from 6.2% in patients with breast cancer to 28.5% in patients with ovarian cancer.

About 12% of patients did not receive primary tumor-directed treatment. This percentage differed largely by cancer type, being lowest for patients with breast cancer (2.5%) and highest for patients with pancreatic (29.7%) and stomach cancer (29.9%). More than 80% of patients with breast cancer underwent surgery in combination with neo- and/or adjuvant therapy. Surgery alone was performed in almost half (49.7%) of the patients diagnosed with colon cancer and 28.6% of patients with rectal cancer.

Table 2 shows SE and SD factors according to patient characteristics. Patients with low and/or middle income were more strongly represented in the older, non-active population. The proportion of patients with high income was higher for women (38.9%) compared with men (31.2%), mainly because of the high proportion of female patients with breast cancer with high income (37.9%). Furthermore, the percentage of patients affected by comorbidities was lower for high-income patients.

The proportion of patients not working because of disability or other reasons before diagnosis was higher for men (27.5%) compared with women (22.7%). Within the non-active population, almost one third of patients (30.5%) were widowed at time of diagnosis and 38.4% of patients in the active population lived alone, being single or separated. Patients who lived with a partner at time of diagnosis were the most highly represented group in both the active (59.0%) and non-active population (54.7%).

The proportion of patients with comorbid conditions was higher in patients either living with a partner or widowed, which represents the majority of the non-active population. In other words, the presence of comorbidities was largely age-dependent. Indeed, the proportion of patients in the non-active population presenting a comorbidity of any type was higher compared with those in the active population. The percentage of females living alone, for any reason, was 53.8% compared with 31.4% in males.

SES and cancer survival

Adjusted HR estimates, including 95% CI, patients at risk and the number of deaths during follow-up are shown in **Fig. 1**. Unadjusted and adjusted HR estimates with 95% CI are provided in Supplementary Table S2.

In the active population, survival was lower for patients with a low or middle household income compared with those with high income. The

Table 2. Patient characteristics by socioeconomic and sociodemographic factors, Belgium 2006–2013.

	Household income			Employment status				Marital status[a]			
	Low	Middle	High	Working	Job-seeking	Disabled/other	Retired	Cohabitating	Separated	Single	Widowed
Patient characteristics	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**
Overall	35,681 (32.6)	35,065 (32.0)	38,845 (35.4)	—	—	—	—	39,656 (56.2)	10,147 (14.4)	6,037 (8.6)	14,695 (20.8)
Age and status at diagnosis											
<65 years and nonretired (active)	9,959 (26.1)	11,234 (29.4)	16,975 (44.5)	25,604 (67.1)	3,252 (8.5)	9,312 (24.4)	—	14,424 (59.0)	5,694 (23.3)	3,678 (15.1)	640 (2.6)
65+ years or retired (nonactive)	25,722 (36.0)	23,831 (33.4)	21,870 (30.6)	—	—	—	71,423 (100.0)	25,232 (54.7)	4,453 (9.7)	2,359 (5.1)	14,055 (30.5)
Mean age (standard deviation)	*69.5 (12.6)*	*67.8 (13.0)*	*63.8 (13.1)*	*51.6 (7.6)*	*52.4 (6.7)*	*55.6 (7.5)*	*74.6 (8.1)*	*65.9 (12.1)*	*61.6 (10.7)*	*58.7 (15.2)*	*77.9 (9.4)*
Sex											
Male	17,622 (35.7)	16,357 (33.1)	15,406 (31.2)	8,419 (63.5)	1,190 (9.0)	3,652 (27.5)	36,124 (50.6)	21,666 (68.6)	4,009 (12.7)	2,486 (7.9)	3,432 (10.9)
Female	18,059 (30.0)	18,708 (31.1)	23,439 (38.9)	17,185 (69.0)	2,062 (8.3)	5,660 (22.7)	35,299 (49.4)	17,990 (46.2)	6,138 (15.8)	3,551 (9.1)	11,263 (28.9)
Comorbidity[b]											
Chronic respiratory	3,100 (8.7)	3,108 (8.9)	2,375 (6.1)	847 (3.3)	133 (4.1)	858 (9.2)	6,745 (9.4)	3,380 (8.5)	845 (8.3)	356 (5.9)	1,152 (7.8)
Chronic cardiovascular	18,445 (51.7)	18,294 (52.2)	17,136 (44.1)	5,608 (21.9)	683 (21.0)	3,091 (33.2)	44,493 (62.3)	20,196 (50.9)	4,144 (40.8)	2,132 (35.3)	10,286 (70.0)
Diabetes mellitus	5,070 (14.2)	4,947 (14.1)	4,227 (10.9)	1,233 (4.8)	205 (6.3)	1,003 (10.8)	11,803 (16.5)	5,531 (13.9)	1,065 (10.5)	597 (9.9)	2,592 (17.6)

[a]Marital status was only available for incidence years 2009–2013. Overall percentages by income and marital status category are provided in the first row.
[b]Comorbidity data were extracted from the administrative databases of the health insurance companies and referred to patients treated before cancer diagnosis.

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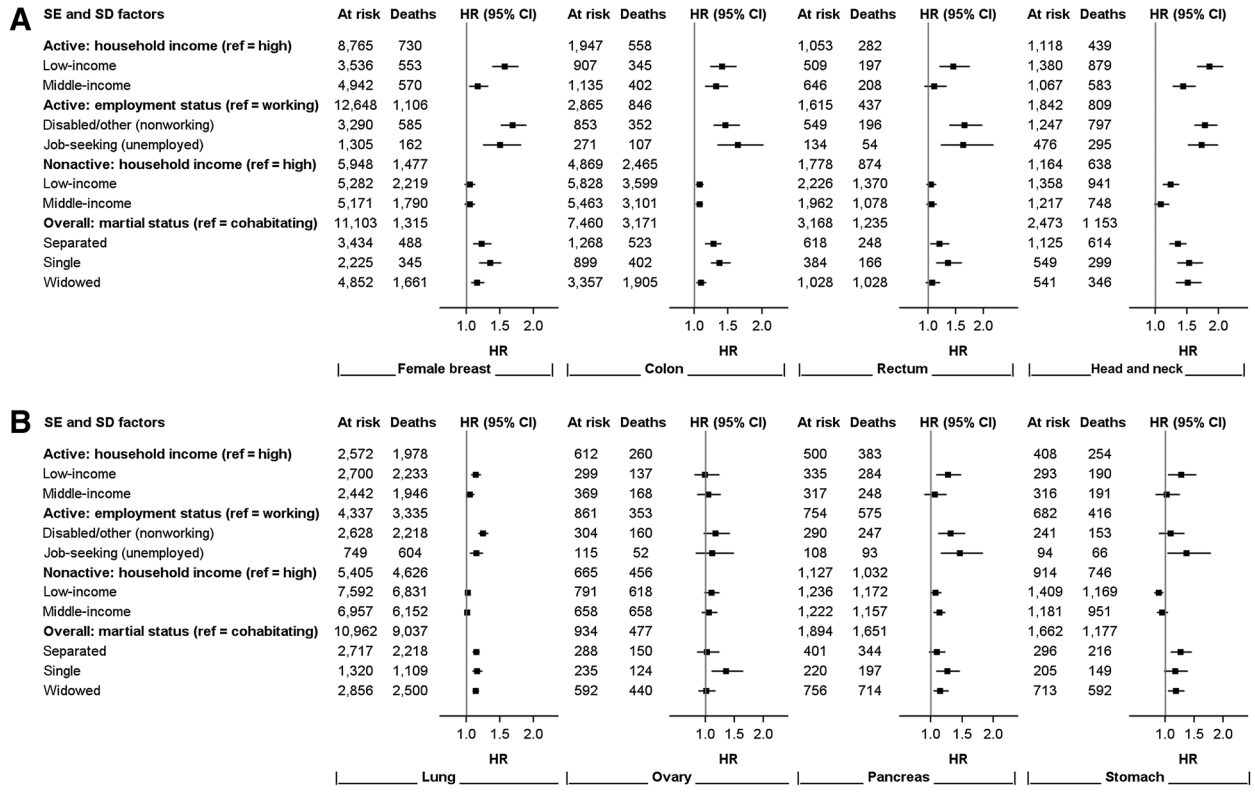

Figure 1.

Adjusted hazard ratios (HR) by socioeconomic (SE) and sociodemographic (SD) factors and cancer type: female breast, colon, rectal, and head and neck cancers (**A**); lung, ovarian, pancreatic, and stomach cancers (**B**). HR estimates are provided with 95% confidence intervals (CI) and were adjusted for age, sex (if applicable), stage, subtype (if applicable), chronic respiratory and cardiovascular comorbidities, diabetes mellitus, and primary treatment scheme. Active: patients ages less than 65 years at diagnosis and nonretired; Nonactive: patients ages at least 65 years or retired. Marital status was only available for incidence years 2009–2013.

association was most pronounced for colon (HR_{low}, 1.41; 95% CI, 1.23–1.62; HR_{middle}, 1.32; 95% CI, 1.16–1.50), breast (HR_{low}, 1.57; 95% CI, 1.38–1.77; HR_{middle}, 1.17; 95% CI, 1.04–1.32) and head and neck cancers (HR_{low}, 1.85; 95% CI, 1.65–2.07; HR_{middle}, 1.44; 95% CI, 1.27–1.63). For patients diagnosed with rectal, lung, pancreatic, and stomach cancer, survival was lower for patients with low income. No association between survival and income was found for ovarian cancer. Within the non-active population, low (HR_{low}, 1.08; 95% CI, 1.02–1.14) and middle-income categories (HR_{middle}, 1.08; 95% CI, 1.02–1.13) showed a statistically significant lower survival for colon cancer, whereas for head and neck (HR_{low}, 1.24; 95% CI, 1.12–1.37) and pancreatic cancer (HR_{middle}, 1.13; 95% CI, 1.04–1.23), only patients with low income or middle income seemed to have a poorer survival compared with high-income patients, respectively.

Not working was associated with worse survival for all cancer types, except ovarian cancer. Both job-seeking and not working because of disability/incapacity or other reasons were found to be statistically significantly associated with poorer survival compared with being employed, with the exception of stomach cancer (only job-seeking). The strongest association was observed in head and neck cancers ($HR_{not\text{-}working}$, 1.78; 95% CI, 1.61–1.97; $HR_{job\text{-}seeking}$, 1.73; 95% CI, 1.51–1.98), followed by rectal ($HR_{not\text{-}working}$, 1.65; 95% CI, 1.38–1.98; $HR_{job\text{-}seeking}$, 1.63; 95% CI, 1.23–2.18), colon ($HR_{not\text{-}working}$, 1.46; 95% CI, 1.28–1.67; $HR_{job\text{-}seeking}$, 1.64; 95% CI, 1.34–2.02) and female breast cancer ($HR_{not\text{-}working}$, 1.69; 95% CI, 1.51–1.89; $HR_{job\text{-}seeking}$, 1.50; 95% CI, 1.25–1.81). For lung ($HR_{not\text{-}working}$, 1.25; 95% CI, 1.18–1.32; $HR_{job\text{-}seeking}$, 1.15; 1.05–1.25) and pancreatic cancer ($HR_{not\text{-}working}$:1.31 [1.11–1.55], $HR_{job\text{-}seeking}$, 1.46; 95% CI, 1.16–1.83), this association was less pronounced, though statistically significant.

Marital status was also associated with cancer survival. Overall, living alone was associated with worse survival than being married or cohabitating. We found worse survival for single, separated, and widowed patients across all cancer types, except for stomach (only separated and widowed), ovarian (only singles), pancreatic (only singles and widowed), and rectal cancer (only separated and singles). The largest differences were observed for head and neck cancer ($HR_{separated}$, 1.35; 95% CI, 1.22–1.49; HR_{single},1.53; 95% CI, 1.34–1.75; $HR_{widowed}$, 1.51; 95% CI, 1.32–1.73), colon cancer ($HR_{separated}$, 1.28; 95% CI, 1.16–1.40; HR_{single}, 1.37; 95% CI, 1.24–1.53; $HR_{widowed}$, 1.10; 95% CI, 1.03–1.18) and female patients with breast cancer ($HR_{separated}$, 1.23; 95% CI, 1.10–1.37; HR_{single}, 1.35; 95% CI, 1.19–1.52; $HR_{widowed}$, 1.16; 95% CI, 1.07–1.27). Again, for patients with lung cancer ($HR_{separated}$, 1.15; 95% CI, 1.09–1.20; HR_{single}, 1.16; 95% CI, 1.09–1.24; $HR_{widowed}$, 1.14; 95% CI, 1.09–1.19), the associations were less pronounced, though statistically significant.

Sensitivity analyses

The association between survival and income was most pronounced for individual income, followed by household, and neighborhood-level income, respectively. This association was higher in the active compared with the non-active population (Supplementary Table S3). Survival models without stage at diagnosis and comorbid conditions

Published OnlineFirst October 20, 2020; DOI: 10.1158/1055-9965.EPI-20-0721

did not result in substantial changes in the survival estimates (Supplementary Table S4), whereas the association between SES and observed survival was less pronounced, though statistically significant, when removing primary treatment as adjustment factor. This was especially the case for employment and marital status (Supplementary Table S5).

Discussion

Evidence of SES-associated disparities in cancer survival have been reported in many countries and for many cancer types (6, 7). The present study is the first to investigate the association between SE and SD factors and cancer survival at the individual-level in Belgium, including more than 100,000 patients diagnosed with 8 common cancer types between 2006 and 2013. Besides patient age, gender and tumor characteristics, survival estimates were adjusted for three major comorbidities (chronic respiratory disease, chronic cardiovascular diseases, and diabetes mellitus) and primary cancer treatment scheme.

Being a complex societal concept, SES consists of cultural, social, and economic dimensions. No single variable adequately captures SES (23, 24). Composite deprivation indexes integrate multiple dimensions of SES, but neither distil the contribution of each factor nor the variation in association (25). To date, most studies that focused on cancer survival considered SES at the area-level (26, 27). However, the size of the geographic unit, and consequently the population heterogeneity, in addition to the index construct, can have major effects on the observed inequalities. As a result, area-level SES may not correspond to the individual SES (28, 29). By investigating multiple SE and SD dimensions separately at the individual-level, this study aimed to provide novel insights into how these factors are associated individually with cancer survival in Belgium, without ecological bias (30), and correcting for differences in case-mix.

As a proxy for standard of living, we included a weighted income indicator accounting for differences in household composition and size, which yielded a representative income by household. The research results showed that income was significantly associated with survival for most cancer types, especially in the younger, active population. Financial difficulties could be associated with lifestyle habits that negatively affect health, and furthermore, could alter the optimal and timely use of healthcare services. In addition, although the healthcare system in Belgium is largely tax-funded (31), more affluent patients might disproportionally benefit from advancements in medicine through financial and social connections, and resulting knowledge (11).

Several studies have separately examined the associations of individual and neighborhood deprivation with cancer survival (or mortality). Consequently, it has been suggested that both are independently associated, and could also interact (10, 29, 32, 33). In a Supplementary Analysis, we observed that the association between survival and income was most pronounced for individual income, followed by household, and neighborhood-level income, respectively.

Not-working was negatively associated with cancer survival. Importantly, this association persisted after controlling for stage and comorbid conditions, limiting at least partially the potential health selection bias (34). However, important job-related aspects were not available (i.e., job type, occupational exposures, psychological, and physical factors). We assessed the potential mediator effect of stage at diagnosis and comorbid conditions by removing those adjustment factors in the analyses, resulting in no substantial changes in the survival estimates.

Many studies have suggested that living together/cohabitating has beneficial effects for most patients with cancer, independent of age, which could be assigned to stronger social support and healthier lifestyle (35). In agreement with international studies (3, 23, 36), our study showed that being single, divorced, or widowed affected cancer survival negatively for most cancer types.

In the present study, differences in cancer survival according to SES were most pronounced for head and neck, female breast, and colorectal cancer. These Belgian results correspond with international studies reporting strong associations between SES and survival among patients diagnosed with a cancer with good to intermediate overall prognosis (such as female breast cancer), and certain life-style–related cancer types (e.g., head and neck cancers; refs. 25, 37, 38). The association between SE and SD factors and survival among patients with lung cancer were statistically significant but less pronounced compared with other lifestyle-related cancers, which confirms results of previous studies in other populations (35), suggesting that for cancers with poor prognosis, such as lung and pancreatic cancer, there might be less potential impact of SES (1, 39–41).

Although screening programs in Belgium exist for breast and colorectal cancer, information on participation in screening was not available. For both cancer types, SE and SD factors were strongly associated with survival in this study. In line with international observations, a lower uptake of screening for lower SES groups might also be possible in Belgium (42). Nevertheless, other researchers have observed SE inequities in cancer survival for both screen-detected and non–screen-detected groups, independent of stage at diagnosis (38).

Reasons behind the observed disparities are multiple and complex and should be further examined. The absence of survival disparities according to SES in clinical trials (43–45) suggests that lower survival among deprived patients in the general population, as observed in our study, may be due to healthcare factors. Delay in diagnosis and treatment, thoroughness of diagnostic investigation, access to optimal care and complications of treatment might be different between deprived and affluent patients in a real-world situation (1, 46). Besides healthcare-related factors, differences in health-consciousness, health-seeking behaviors, or social support and connections might play a role and can be presumed to be more important in the current study given the high-level and accessible healthcare setting in our country. Health policy interventions need to consider the observed deprivation gap to plan targeted actions and to further promote equity in health, health awareness, and treatment adherence.

Our study presented several limitations. Income is associated with age and gender. It is less stable than other dimensions of SES, for example, educational attainment, and cannot be set on equal terms with wealth or self-assessed financial status, especially in the older population. Data on education, occupation, and *de facto* living situation would have provided additional insights on how SES interplays with cancer survival. Unfortunately, these data were not available. The integration of all three SE or SD factors into one model would have provided information on how these factors interact with each other and survival; however, these models would have lacked other dimensions of SES, and hence still provided a partial view of the relationship between SES and cancer survival. We therefore chose to study each SE or SD factor separately, taking clinical characteristics and treatment into account. A cross-tabulation of household income, employment, and marital status is provided in Supplementary Material (S6).

Origins and mechanisms leading to inequalities in health are multifaceted; besides clinical patient and tumor characteristics, residual confounding from lifestyle factors is likely present. No information regarding alcohol and tobacco consumption, nutrition,

physical activity, obesity, psychosocial and mental health, social support, health consciousness or healthcare seeking behaviors was available (20, 34, 47–49). Furthermore, information on molecular markers, which affect available treatment options and prognosis in different cancer types, were unavailable.

A high proportion of patients with pancreatic cancer presented with diabetes mellitus. However, the relationship between diabetes and pancreatic cancer is complex and intertwined: Although diabetes is an important risk factor for pancreatic cancer, new onset diabetes may be an early symptom of yet undetected pancreatic cancer (50).

The treatment data refer to the received primary treatment scheme, which does not necessarily reflect the intended treatment. Furthermore, treatment was not considered as a time-varying covariable but at baseline (51). However, the effect of treatment as an additional adjustment factor was assessed in sensitivity analyses; the association between SES and survival remained statistically significant but was less pronounced, especially for employment and marital status.

Several studies observed trends in cancer survival disparities according to SES (5, 52, 53). In our study, sensitivity analyses considered the inclusion of the year of diagnosis as an additional adjustment factor. However, this variable was non-significant and excluded from the final analyses. Future research should consider a larger observation period to perform trend analyses.

The number of patients with cancer who died within 5 years after diagnosis varied largely by cancer type and patient characteristics. For some cancer types (i.e., ovary, pancreas and stomach), low numbers of death in some categories necessitate cautious interpretation of results.

Despite a comprehensive and nationwide health insurance program where equity in rights and access to healthcare are pursued, SES is a significant determinant of cancer survival in Belgium. Although differences in patient and tumor characteristics at least partially explained the association between SE and SD factors and cancer survival, household income, employment, and marital status remained associated with cancer survival for most cancer types. The magnitude of the association between SE and SD factors and cancer survival differed by cancer type and was most prominent for certain lifestyle-related cancer types (e.g., head and neck cancers) and those with good to moderate prognosis (e.g., female breast cancer and colorectal cancer). By providing new and substantial aspects, this study aims to build a more comprehensive picture of cancer epidemiology in Belgium and to provide new insights on how to tackle SE disparities in cancer survival.

Authors' Disclosures

M. Rosskamp reports grants from Kom op tegen Kanker during the conduct of the study. J. Verbeeck reports grants from Kom op tegen Kanker during the conduct of the study. S. Gadeyne reports other from Vrije Universiteit Brussel during the conduct of the study. F. Verdoodt reports grants from Kom op tegen Kanker during the conduct of the study. H. De Schutter reports grants from Kom op tegen Kanker during the conduct of the study. No disclosures were reported by the other authors.

Authors' Contributions

M. Rosskamp: Conceptualization, software, formal analysis, funding acquisition, validation, methodology, writing-original draft, project administration, writing-review and editing. **J. Verbeeck:** Data curation, formal analysis, writing-review and editing. **V. Sass:** Validation, writing-review and editing. **S. Gadeyne:** Conceptualization, supervision, validation, methodology, writing-review and editing. **F. Verdoodt:** Conceptualization, resources, supervision, funding acquisition, validation, methodology, project administration, writing-review and editing. **H. De Schutter:** Conceptualization, resources, supervision, funding acquisition, validation, writing-review and editing.

Acknowledgments

M. Rosskamp, J. Verbeeck, F. Verdoodt, and H. De Schutter had been awarded a grant from Kom op tegen Kanker (KOTK). The authors would like to thank KOTK for funding this research; the Crossroads Bank for Social Security, Intermutualistic Agency (IMA), and eHealth for data preparation, delivery, and linkage; Gilles Macq and Geert Silversmit (Belgian Cancer Registry) for their statistical expertise; and Hanna Peacock (Belgian Cancer Registry) for proofreading the article.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received May 25, 2020; revised August 28, 2020; accepted October 9, 2020; published first October 20, 2020.

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Published OnlineFirst October 20, 2020; DOI: 10.1158/1055-9965.EPI-20-0721

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Michael Rosskamp, Julie Verbeeck, Victoria Sass, et al.

Cancer Epidemiol Biomarkers Prev Published OnlineFirst October 20, 2020.