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Title page

Occupational disparities in site-specific cancer survival in Korean women

Running title: Cancer survival by occupation in Korean women

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ABSTRACT

Objectives: We sought to examine occupational disparities in cancer survival among Korean women.

Design: Population-based, registry-linkage study

Setting: South Korea

Participants: Our study population comprised female workers registered in the Korean national employment insurance program during 1995-2000 and diagnosed with cancer between 1995-2008. A total of 61,110 women with cancer diagnoses was included in analysis. The occupation was categorized into 4 groups: i) managers, professionals, and technical workers, ii) clerks, iii) service/sales workers, iv) blue-collar workers.

Primary and secondary outcome measure: Study population were linked to the national death registry until 2009. Hazard ratios for mortality adjusting for age and year of diagnosis were calculated using managers and professionals as the reference.

Results: Women in service/sales (HR 1.25, 95% CI 1.15-1.35) and blue-collar occupations (HR 1.41, 95% CI 1.14-1.77) had lower survival for all cancer sites combined, while blue-collar workers showed lower survival for lung (HR 1.41, 95% CI 1.14-1.77), breast (HR 1.28, 95% CI 1.06-1.54), cervical cancer (HR 1.42, 95% CI 1.02-2.06) and non-Hodgkin lymphoma (HR 1.54, 95% CI 1.03-2.40) compared to women in professional and managerial positions.

Conclusion: We found substantial and significant inequalities in cancer survival by the occupational group among Korean women, even in the context of universal access to cancer screening and treatment.

Keywords Socioeconomic Factors; Occupations; Lung Neoplasm; Breast Neoplasms; Uterine Cervical Neoplasms; Thyroid Neoplasms; Lymphoma, Non-Hodgkin

Strengths and limitations of this study

- This is the first study to investigate occupational disparities in cancer survival among Korean women.
- Using a large and representative workers cohort and cancer registry data enabled us to analyze a number of specific cancer sites with a sufficient number of cases, and to generalize the results to the population of working women in Korea
- Due to our longitudinal follow-up design, reverse causation of cancer diagnosis resulting in a change in occupation can be ruled out.
- Due to the lack of information on important covariates, we could not evaluate the contribution of mediating variables between occupation and cancer survival

Occupational disparities in site-specific cancer survival in Korean women

INTRODUCTION

Cancer is a leading cause of death in South Korea, with more than 200,000 new cancer cases diagnosed each year[1]. Significant socioeconomic inequalities in cancer survival have been previously found in many countries despite universal access to health care[2–4]. As an indicator of socioeconomic status (SES), the occupation has been widely used, especially in European countries[5]. However, studies on occupational disparities in cancer survival remain sparse in the Asian context[6–8].

Cancer incidence, mortality, and survival are key measures of cancer burden, and the use of all three measures can provide a more comprehensive picture in assessing progress in the context of a national cancer control strategy[9]. According to a previous Korean study of occupational disparities in cancer incidence, women with high SES occupations showed a significantly higher incidence of all cancers compared to women with lower SES occupations[10]. However, cancer mortality was lower among high SES women than among lower SES women[11]. These findings suggest the need for further clarification of survival differences across occupational strata among Korean women.

The mechanisms linking SES disparities in cancer survival include factors such as stage at diagnosis, access to treatment modalities, and patient characteristics (e.g. treatment adherence)[12]. Women working in high SES occupations may participate in cancer screenings more frequently than low SES women. A number of studies have also pointed to differences in access to treatment between different socioeconomic groups[13]. Also, patients' characteristics such as comorbidity, nutritional status, social support, and adherence behavior might influence disparities in cancer survival[13]. According to a Danish population-based study, women in high SES occupations experienced a higher incidence of breast cancer than low SES women, but the pattern was reversed for breast cancer survival[14]. Earlier diagnosis and better treatment are determinants of better survival of breast cancer among women with high SES occupations, while reproductive factors such as late age at first birth and fewer children can explain their higher incidence. Korean data also showed a higher incidence of breast cancer among managers and professionals than among blue-collar workers[10].

In South Korea, several studies have been published on socioeconomic disparities in cancer survival, but most of these studies did not show sex-stratified results and occupation was not used as an indicator to measure SES[15–17]. A previous study limited in a local area performed sex-stratified analysis, however, the SES indicator used was ecological, based on an area-level deprivation index[18].

Thus, in the present study, we aimed to investigate occupational disparities on cancer survival among Korean working women using large longitudinal data.

METHODS

Data source and study population

Our data were derived from a cohort of Korean workers, who were covered by the national Employment Insurance program (1995-2000). The Korean Employment Insurance system started in 1995, covering companies with more than 70 employees, and was expanded to cover all employed workers in the private sector regardless of company size since 1998. The database included 11,435,937 workers. We excluded foreign workers, workers under the age of <15 years or >60 years at baseline, and workers with inaccurate enrollment dates. We restricted the study sample to women with valid occupational information and who had held the same occupation during 1995-2000.

Cancer cases were confirmed by matching employees to the Korea Central Cancer Registry (KCCR) (1995-2008). Diagnoses of malignant neoplasms (C00-C97) based on the International Classification of Disease, 10th Revision (ICD-10), was used to code specific cancer sites. Individuals diagnosed with cancer before enrollment in the workers' cohort or having an inaccurate date of diagnosis were excluded from the analysis. As a result, 61,110 female cancer cases were used for analysis (Figure 1).

Calculation of survival

The study population was followed via linkage to the death registry operated by the Korea National Statistical Office (KNSO) between 1995 and 2009. The average follow-up was 4.2 person-years. We used overall survival as an outcome which was calculated from the date of cancer diagnosis to the date of death regardless of the cause of death.

Classification of occupations

To classify occupations, we used the information on occupation from the employment insurance program coded using the Korean Standard Classification of Occupations (KSCO) between 1995 and 2000. This classification corresponds to the International Standard Classification of Occupations[11]. To compare between occupations with a sufficient number of cases, we collapsed the nine occupational categories into four groups as follows: 1) Group1 (managers, professionals, and technical workers): KSCO1 (legislators, senior officials, and managers), KSCO2 (professionals) and KSCO3 (technicians and associate professionals), 2) Group 2 (Clerks): KSCO4 (clerks), 3) Group 3 (Service and sales workers): KSCO5 (service workers and sale workers), 4) Group 4 (Blue-collar workers): KSCO6 (agricultural, forestry, and fishery workers), KSCO7 (craft and related trades workers), KSCO8 (plant and machine operators, and assemblers) and KSCO9 (elementary occupations)[11].

Statistical analysis

Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% confidence intervals (95% CIs) adjusting for age and year of diagnosis as continuous variables to investigate the disparities across occupational groups. As screening & treatment have improved over time for many cancer sites, we adjusted for year of diagnosis in the Cox hazard models. The outcomes analyzed included all cancer sites combined (C00-C97) as well as the ten commonest cancer sites which had sufficient cases. Survival curves are shown for all cancer sites combined as well as specific sites that showed statistically significant disparities by occupation.

Patient or public involvement

No patient involved.

RESULTS

Table 1 summarizes the characteristics of female cancer cases used for analysis. Among a total of 61,110 cancer cases, 28.2% were diagnosed with cancer in their 40s. Around half of the study sample were employed in Group 4 occupation (Blue-collar workers). During the follow-up period, 13,541 (22.2%) women died. The most frequently diagnosed cancer sites were thyroid (25.0%), breast (20.7%), and stomach (11.3%).

1 **Table 1. Characteristics of the study population**

		N	%
Total		61110	100.0
Age of diagnosis	<20	72	0.1
	20-29	5245	8.6
	30-39	15579	25.5
	40-49	17216	28.2
	50-59	15005	24.6
	60-	7993	13.1
Year of diagnosis	1995-1999	6654	10.9
	2000-2004	21861	35.8
	2005-2008	32595	53.3
Occupational group	Group 1 (Managers, professionals and technical workers)	5822	9.5
	Group 2 (Clerks)	15362	25.1
	Group 3 (Service and sales workers)	7524	12.3
	Group 4 (Blue-collar workers)	32402	53.0
Vital status	Alive	47569	77.8
	Dead	13541	22.2
Cancer sites	Lip, oral cavity, and pharynx (C00-C14)	579	0.9
	Esophagus (C15)	59	0.1
	Stomach (C16)	6918	11.3
	Colon, rectosigmoid junction, rectum (C18-C20)	4721	7.7
	Liver and intrahepatic bile ducts (C22)	2026	3.3
	Gallbladder, other and unspecified parts of biliary tract (C23-C24)	850	1.4
	Pancreas (C25)	605	1.0
	Larynx (C32)	33	0.1
	Trachea, bronchus, and lung (C33-C34)	2077	3.4
	Mesothelioma (C45)	24	0.0
	Breast (C50)	12673	20.7
	Cervix uteri (C53)	5271	8.6
	Corpus uteri (C54)	1416	2.3
	Ovary (C56)	1916	3.1
	Kidney (C64)	585	1.0
	Bladder (C67)	245	0.4
	Brain and other parts of central nervous system (C70-C72)	687	1.1
	Thyroid gland (C73)	15295	25.0
	Hodgkin lymphoma (C81)	79	0.1

Non-Hodgkin lymphoma (C82-C85, C96)	1209	2.0
Multiple myeloma (C90)	198	0.3
Leukemia (C91-C95)	1043	1.7

Hazard ratios (HRs) and 95% confidence intervals (CIs) of cancer survival using Group 1 (managers, professionals and technical workers) as the reference group are presented in Table 2.

Table 2. Hazard ratios and their 95% Confidence intervals by occupational groups using Cox proportional hazard model

		Hazard Ratio[a)]	95% Confidence interval	
All cancer (C00-C97)	Group 1	Ref		
	Group 2	**1.08**	**1.00**	**1.17**
	Group 3	**1.25**	**1.15**	**1.35**
	Group 4	**1.41**	**1.14**	**1.77**
Stomach (C16)	Group 1	Ref		
	Group 2	1.06	0.9	1.26
	Group 3	1.16	0.97	1.39
	Group 4	1.09	0.94	1.28
Colorectal (C18-C20)	Group 1	Ref		
	Group 2	0.97	0.75	1.25
	Group 3	0.97	0.74	1.28
	Group 4	1.02	0.83	1.29
Liver (C22)	Group 1	Ref		
	Group 2	0.94	0.71	1.26
	Group 3	1.08	0.82	1.44
	Group 4	1.23	0.98	1.58
Lung (C33-C34)	Group 1	Ref		
	Group 2	1.21	0.94	1.58
	Group 3	1.15	0.88	1.5
	Group 4	**1.41**	**1.14**	**1.77**
Breast (C50)	Group 1	Ref		
	Group 2	1.17	0.96	1.42
	Group 3	1.13	0.91	1.42
	Group 4	**1.28**	**1.06**	**1.54**
Cervix uteri (C53)	Group 1	Ref		
	Group 2	1.21	0.82	1.82
	Group 3	1.37	0.94	2.05
	Group 4	**1.42**	**1.02**	**2.06**
Corpus uteri (C54)	Group 1	ref		
	Group 2	1.56	0.79	3.29
	Group 3	1.73	0.85	3.72
	Group 4	1.45	0.81	2.87
Ovary (C56)	Group 1	ref		
	Group 2	0.92	0.64	1.35

	Group 3	1.23	0.83	1.85
	Group 4	1.21	0.87	1.73
Thyroid (C73)	Group 1	Ref		
	Group 2	1.27	0.58	3.05
	Group 3	**2.22**	**1.02**	**5.36**
	Group 4	**2.05**	**1.05**	**4.62**
Non-Hodgkin lymphoma (C82-C85, C96)	Group 1	ref		
	Group 2	1.38	0.89	2.22
	Group 3	1.37	0.84	2.26
	Group 4	**1.54**	**1.03**	**2.40**

Group 1, Managers, professionals and technical workers; Group 2, Clerks; Group 3, Service and sales workers; Group 4, Blue-collar workers

a) Adjusted by age and year of diagnosis

Blue-collar workers (HR 1.41, 95% CI 1.14-1.77) and Service/sales workers (HR 1.25, 95% CI 1.15-1.35) showed poorer survival for all cancer sites combined. In terms of site-specific survival, blue-collar workers showed poorer survival for lung, breast, cervix uteri, and non-Hodgkin lymphoma. Both Blue-collar workers and service/sales workers showed significantly worse survival for thyroid cancer. Most other cancer sites (except for colorectal cancer) showed better survival for high SES occupation (managers, professionals and technical workers) as well, although the difference across occupational groups was not statistically significant.

Survival curves for all cancer combined and selected cancer sites by occupational groups are presented in Figure 2. Due to extremely high survival among thyroid cancer patients, absolute differences in survival across occupational groups were not found.

DISCUSSION

To our knowledge, this is the first Korean study to comprehensively document occupational disparities in cancer survival in a female working population.

In the previous studies on socioeconomic cancer disparities, cancer of good prognosis showed a wider difference across SES groups[4,7,17]. Significant disparities in survival for breast, cervix uteri, thyroid cancer and non-Hodgkin lymphoma found in the present study are in line with those previous studies. Our findings are consistent with the "fundamental cause" theory of socioeconomic disparities advanced by Link and Phelan[19]. According to this theory, socioeconomic disparities in health arise due to differential access to and deployment of a variety of flexible resources to benefit health, including not only money and knowledge, but also symbolic prestige and powerful social connection by people with higher SES. Thus, it can be hypothesized that strong socioeconomic gradients in survival would be observed for cancer sites with a good prognosis, i.e., deaths which are highly preventable because effective modalities exist for early diagnosis and cure. On the other hand, fundamental cause theory predicts that SES disparities would be small or non-existent for cancers which have a uniformly poor prognosis and where effective screening is unavailable, where high SES people cannot utilize their resources.

Although lung cancer is often fatal for patients, it showed significant disparities as well in our data, showing a similar magnitude of difference across occupational groups with all cancer and cervix uteri cancer. As in other cancer sites, the main determinant of social disparities on lung cancer survival is known to be the stage at diagnosis and difference in treatment [20]. Medical cost for lung cancer was 3rd highest among all cancer sites in Korea

[21]. Although Korea has universal health care system under National Health Insurance (NHI) or Medicaid program, patients still had to co-pay 20% of the cost of cancer treatment until 2005 (covered by our follow-up period), in which year the policy of decreasing cancer patients' co-payment to 10%. In a previous Korean study, utilization of inpatient and outpatient medical care of high-income cancer patients was more frequent than low-income patients, and the patients with higher incomes tend to use services from major tertiary hospitals[22]. Thus quality or differences in intensity of medical treatment could be a factor contributing to disparities in lung cancer survival[12].

Social disparities in cancer survival can be also attributed to differences in stage at diagnosis[13]. For the early detection of breast cancer and cervical cancer, the National Cancer Screening Program (NCSP) in Korea provides a mammogram and Pap smear every other year[23]. Despite the free access to screening, income and educational disparities in the uptake of screening continue to persist; the percentage of breast cancer screened population within the past two years were 36.2% in the lowest income group and 42.9% in the highest income group; and for cervical cancer, 43.2% and 65.1% respectively in 2005[24].

Besides NCSP, private health check-ups including cancer screening of which cost is paid fully by the examined individual have been prevalent in Korea. Many companies, usually larger than medium size, pay the fee of these check-ups for employees as a part of the well-fare system. According to a previous study, private cancer screening participation rate was higher in female office workers than in manual workers[25]. According to a previous Korean study, the lowest income group showed 1.35 times higher risk of advanced stage at the time of breast cancer diagnosis than the highest income group[26]. The difference in stage at diagnosis could explain our finding of significant disparities in the survival of breast and cervical cancer.

The current study found the widest relative gap for thyroid cancer survival across occupational groups. There has been a sharp rise in thyroid cancer incidence in Korea, attributed to screening and over-diagnosis[27]. Although thyroid cancer survival was higher in high SES occupations, the incidence was also significantly higher in the same occupational group in the previous study with the same data source[10]. Generally, thyroid cancer survival in Korean women is extremely high, more than 98% 5-year survival rate since 2001[1]. Indeed, the absolute differences between occupational groups during the follow-up period were not observable in survival curves due to extremely low mortality across all occupational groups. Considering the clear opposite trend of the occupational gradient in incidence and survival, and the very low mortality, the finding of thyroid cancer survival disparities might be partly due to over-diagnosis which first started among high SES women.

Although clinical factors such as stage at diagnosis and treatment are observed as the most important determinants of cancer survival social disparities, a number of studies found persistent SES disparities in survival even after adjusting for stage and treatment[12]. Psychosocial factors associated with SES are also considered to play a role in cancer survival, e.g. the impact of social support on breast cancer survival[28].

Our findings with regards to occupational disparities on all cancer survival in women are in line with previous findings in men in Korea; HR 1.38, 95% CI 1.33-1.43 for service/sales workers, HR 1.45, 95% CI 1.42-1.48 for blue-collar workers[7]. There was no obvious difference between men and women on risk estimates in all cancer survival disparity, although men had more cancer sites with statistically significant results. By contrast, occupational disparities in cancer incidence or mortality are more substantial in men than in women according to previous Korean studies[10,11]. These findings would seem to suggest that factors related to cancer survival, such as earlier detection and better treatment can be more important factors than factors related to cancer incidence - health behavior (i.e., smoking and alcohol) or occupational carcinogen exposure - for reducing cancer disparities among working women in Korea.

The present study had some strengths. First, using a large and representative workers cohort and cancer registry data enabled us to analyze a number of specific cancer sites with a sufficient number of cases. The database used for this study, the Employment Insurance data and the National Cancer registry are very complete; therefore, the findings of this study are generalizable to the population of working women in Korea. Second, due to our longitudinal follow-up design, we included only incident cases; hence, reverse causation (i.e. cancer diagnosis resulting in a change in occupation) can be ruled out. Third, we classified occupations based on the information from the Employment Insurance data, which is determined by the companies hiring the individuals. This information is expected to be more accurate than the information collected by self-report.

This study also has several limitations. First, due to the lack of information on important covariates including a stage at diagnosis, treatment information, we could not evaluate the contribution of mediating variables between occupation and cancer survival.

Our study sample did not include women who were not in paid employment. Female labor force participation rates were between 47.0-49.5% for all ages in Korea during 1995-2000, the period covered by our data[29]. Thus, the results are not generalizable to all women in Korea. Furthermore, unemployed women and homemakers showed lower participation in cancer screening than employed women according to a previous study[25]. Cancer survival differences might be wider in the general population if we include unemployed women.

In conclusion, we found substantial occupational disparities in cancer survival among Korean working women, particularly in lung, breast, thyroid cancer and non-Hodgkin lymphoma. Further investigation to assess the influence of possible mediators between occupation and cancer survival is warranted. Health policies should enhance access to cancer screening and quality of treatment among cancer patients with lower SES occupations.

Contributors HEL and EAK conceived of the presented idea. HEL designed the study and performed statistical analysis. IK, EAK and MZ participated in its design. HEL wrote the first draft of the manuscript. EAK, MZ and IK critically revised the manuscript. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by the institutional review boards of the Occupational Safety and Health Research Institute and Korea Occupational Safety and Health Agency, Ulsan, Korea.

Data availability statement The datasets generated and analysed during the current study are available from the corresponding author on reasonable request and with permission of Occupational Safety and Health Research Institute.

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Figure Legends

Figure 1 Selection of study population

Figure 2 Survival curves by occupational groups and selected cancer sites

Group 1, Managers, professionals and technical workers; Group 2, Clerks; Group 3, Service and sales workers; Group 4, Blue-collar workers

Adjusted by age and year of diagnosis

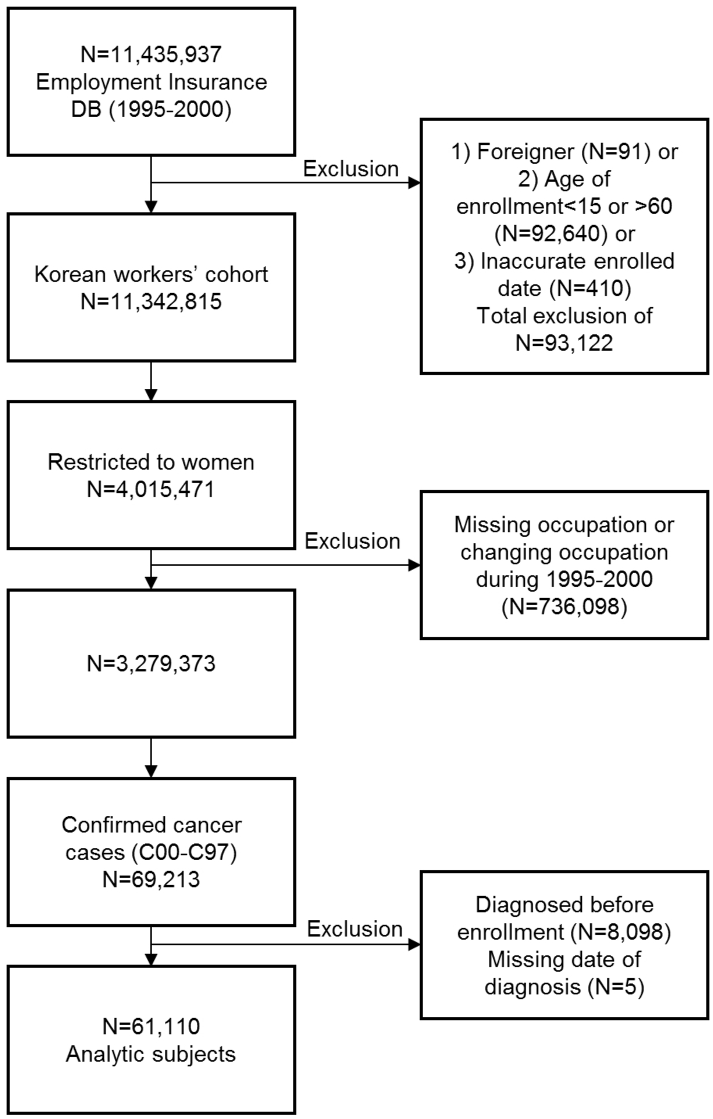

Figure 1 Selection of study population

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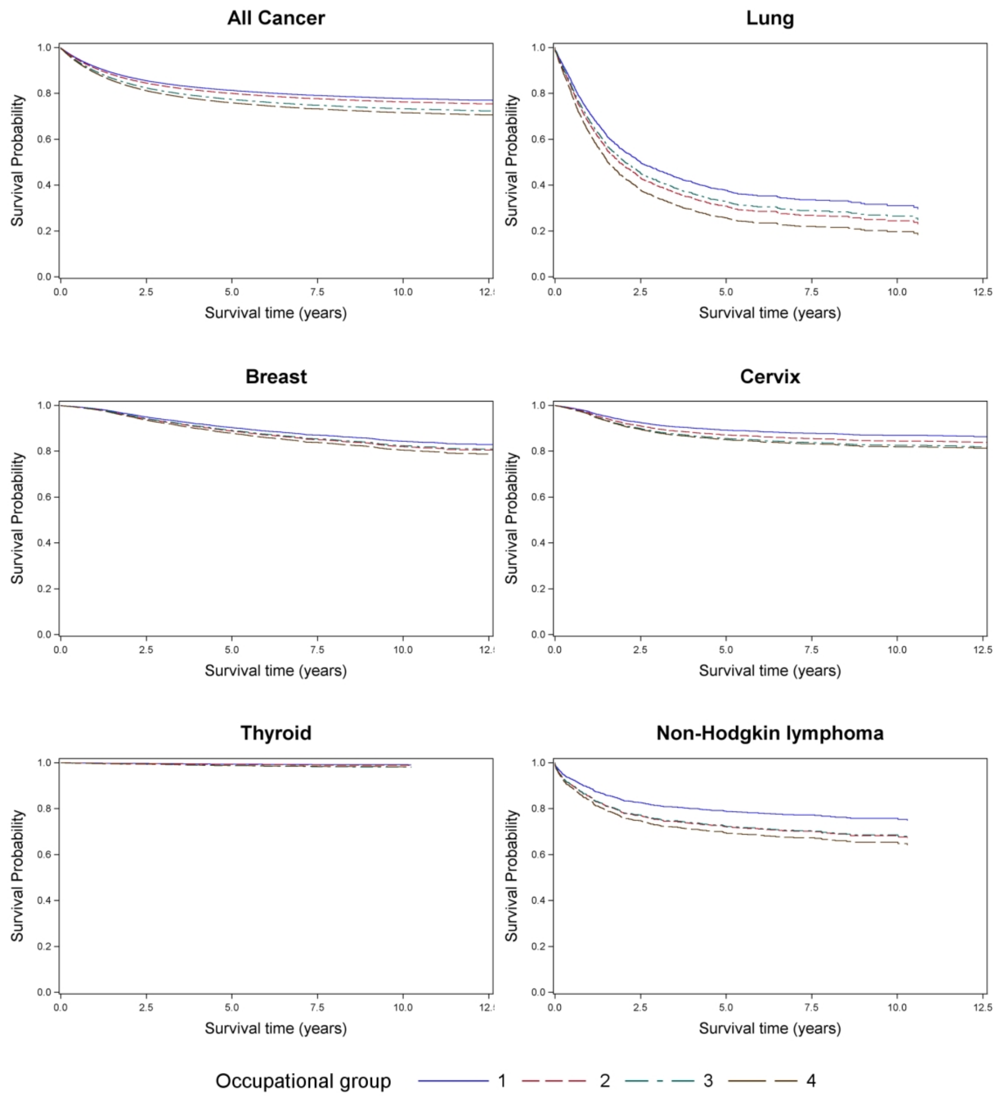

Figure 2 Survival curves by occupational groups and selected cancer sites

175x199mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, explain how loss to follow-up was addressed	6
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	Fig1
		(c) Consider use of a flow diagram	Fig1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
		(c) Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	Report numbers of outcome events or summary measures over time	7-8

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table2
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Fig2
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Occupational disparities in survival in Korean women with cancer: a nationwide registry linkage study

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Title page

Occupational disparities in survival in Korean women with cancer: a nationwide registry linkage study

Running title: Survival by occupation in Korean women with cancer

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Occupational disparities in survival in Korean women with cancer: a nationwide registry linkage study

ABSTRACT

Objectives: We sought to examine occupational disparities in survival among Korean women diagnosed with cancer.

Design: Population-based, registry-linkage study

Setting: South Korea

Participants: Our study population comprised female workers registered in the Korean national employment insurance program during 1995-2000 and diagnosed with cancer between 1995-2008. A total of 61,110 women with cancer diagnoses was included in analysis. The occupation was categorized into 4 groups: i) managers, professionals, and technical workers, ii) clerks, iii) service/sales workers, iv) blue-collar workers.

Primary and secondary outcome measure: Study population were linked to the national death registry until 2009. Hazard ratios for mortality adjusting for age and year of diagnosis were calculated in the study sample and subgroups with 10 specific cancer sites including thyroid, breast, stomach, cervix, colon, or lung cancer using managers, professionals and technical workers as the reference.

Results: Women in service/sales (HR 1.25, 95% CI 1.15-1.35) and blue-collar occupations (HR 1.34, 95% CI 1.25-1.44) had poorer survival for all cancer sites combined, while blue-collar workers showed poorer survival for lung (HR 1.41, 95% CI 1.14-1.77), breast (HR 1.28, 95% CI 1.06-1.54), cervical cancer (HR 1.42, 95% CI 1.02-2.06) and non-Hodgkin lymphoma (HR 1.54, 95% CI 1.03-2.40) compared to women in professional and managerial positions.

Conclusion: We found substantial and significant inequalities in overall survival by the occupational group among Korean women with cancer, even in the context of universal access to cancer screening and treatment.

Keywords Socioeconomic Factors; Occupations; Lung Neoplasm; Breast Neoplasms; Uterine Cervical Neoplasms; Thyroid Neoplasms; Lymphoma, Non-Hodgkin

Strengths and limitations of this study

- This is the first study to investigate occupational disparities in overall survival among Korean women with cancer.
- Using a large and representative workers cohort and cancer registry data enabled us to analyze a number of specific cancer sites with a sufficient number of cases, and to generalize the results to the population of working women in Korea
- Due to our longitudinal follow-up design, reverse causation of cancer diagnosis resulting in a change in occupation can be ruled out.
- Due to the lack of information on important covariates, we could not evaluate the contribution of mediating variables between occupation and survival in cancer patients.

Occupational disparities in site-specific cancer survival in Korean women

INTRODUCTION

Cancer is a leading cause of death in South Korea, with more than 200,000 new cancer cases diagnosed each year[1]. Significant socioeconomic inequalities in cancer survival have been previously found in many countries despite universal access to health care[2–4]. As an indicator of socioeconomic status (SES), the occupation has been widely used, especially in European countries[5]. However, studies on occupational disparities in cancer survival remain sparse in the Asian context[6–8]. These studies reported significantly poorer survival for pancreatic cancer among blue-collar workers and service workers compared to white collar workers, as well as worse survival for bladder cancer among professionals and managers, sales and service workers, construction workers, and workers in manufacturing compared to clerical workers in Japan[6,8]. A previous Korean study showed that men in service/sales and blue-collar occupations had poorer survival for esophagus, stomach, colorectal, liver, larynx, lung, prostate, thyroid cancer and non-Hodgkin lymphoma compared to men in professional and managerial jobs[7].

Cancer incidence, mortality, and survival are key measures of cancer burden, and the use of all three measures can provide a more comprehensive picture in assessing progress in the context of a national cancer control strategy[9]. According to a previous Korean study of occupational disparities in cancer incidence, men showed substantial occupational disparities in lung and liver cancer incidence, but women in professional and managerial jobs showed a significantly higher incidence of all cancers combined and selective cancers including breast, corpus uteri, ovary, or thyroid cancer, compared to women in service and sales or blue-collar jobs [10].

However, cancer mortality was significantly higher among women in elementary occupations than among professionals and managers[11].

Based on these findings, we hypothesized that occupations in lower social positions would be linked to poorer survival in female cancer patients. Occupation – along with educational attainment and income – is considered one of the fundamental axes of social stratification [5]. Occupation influences an individual's access to resources (such as income, savings, retirement pension), access to health insurance, access to paid leave and child care, access to powerful social connections ("social capital"), as well as prestige and status in society. Broadly speaking, the mechanisms linking SES disparities in cancer survival include factors that operate across the cancer spectrum, including stage of diagnosis, access to treatment modalities, and treatment adherence[12]. For example, professional and managerial women may participate in cancer screenings more frequently than blue-collar job women. A number of studies have also pointed to differences in access to treatment between different socioeconomic groups[13]. Also, patients' characteristics such as comorbidity, nutritional status, social support, and treatment adherence behavior might influence disparities in cancer survival[13]. According to a Danish population-based study, women in higher occupational social class experienced a higher incidence of breast cancer than lower occupational social class women, but the pattern was reversed for breast cancer survival[14]. Earlier diagnosis and better treatment are determinants of better survival of breast cancer among women in higher occupational social class, while reproductive factors such as late age at first birth and fewer children can explain their higher incidence. Korean data also showed a higher incidence of breast cancer among managers and professionals than among blue-collar workers[10].

In South Korea, several studies have been published on socioeconomic disparities in cancer-specific or overall survival in cancer patients, but most of these studies did not show sex-stratified results and occupation was not used as an indicator to measure SES[15–17]. A previous study limited in a local area performed sex-stratified analysis, however, the SES indicator used was ecological, based on an area-level deprivation index[18].

Thus, in the present study, we aimed to investigate occupational disparities on survival among Korean working women with cancer using large longitudinal data.

METHODS

Data source and study population

Our data were derived from a cohort of Korean workers, who were covered by the national Employment Insurance program (1995-2000). The Korean Employment Insurance system started in 1995, covering companies with more than 70 employees, and was expanded to cover all employed workers in the private sector regardless of company size since 1998. Thus, the data of Employment Insurance did not include employers, self-employed, unpaid family workers, and employees in the public sector. The database included 11,435,937 workers. We excluded foreign workers, workers under the age of 15 years or >60 years at baseline (on the date of hire), and workers with invalid or incomplete enrollment dates. We restricted the study sample to women with valid occupational information and women who stayed in the same occupation between 1995-2000. After establishing the workers' dataset, cancer cases were confirmed by matching workers to the Korea Central Cancer Registry (KCCR) (1995-2008). Diagnoses of malignant neoplasms (C00-C97) based on the International Classification of Disease, 10th Revision (ICD-10), was used to code specific cancer sites. Individuals diagnosed with cancer before enrollment in the workers' cohort or having an incomplete or missing date of diagnosis were excluded from the analysis. As a result, 61,110 female cancer cases were used for analysis (Figure 1).

The study population was followed via linkage to the death registry operated by the Korea National Statistical Office (KNSO) between 1995 and 2009. The coverage of the death registry can be regarded complete because all deaths in Korea are reported to the KNSO by law.

Classification of occupations

To classify occupations, we used the information on occupation from the employment insurance program coded using the Korean Standard Classification of Occupations (KSCO) between 1995 and 2000. This classification corresponds to the International Standard Classification of Occupations[11]. To compare between occupations with a sufficient number of cases, we collapsed the nine occupational categories into four groups as follows: 1) Group1 (managers, professionals, and technical workers): KSCO1 (legislators, senior officials, and managers), KSCO2 (professionals) and KSCO3 (technicians and associate professionals), 2) Group 2 (clerks): KSCO4 (clerks), 3) Group 3 (service and sales workers): KSCO5 (service workers and sale workers), 4) Group 4 (blue-collar workers): KSCO6 (agricultural, forestry, and fishery workers), KSCO7 (craft and related trades workers), KSCO8 (plant and machine operators, and assemblers) and KSCO9 (elementary occupations)[11]. Based on average income and education distribution, managers, professionals, and technical workers was considered as high SES occupation, and service/sales workers and blue-collar workers were considered as low SES occupations[10].

Statistical analysis

We used overall survival as an outcome which was defined as the time interval between the date of cancer diagnosis and the date of death from any cause or the date of the end of follow-up (December 31st, 2009), whichever came first. Cancer patients who were not matched with death registry were considered alive and were censored at the end of study. The average follow-up was 4.2 person-years.

Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% confidence intervals (95% CIs) adjusting for age and year of diagnosis as continuous variables to investigate the disparities across occupational groups. As screening & treatment have improved over time for many cancer sites, we adjusted for year of diagnosis in the Cox hazard models. The outcomes analyzed included all cancer sites combined (C00-C97) as well as the ten commonest cancer sites which had sufficient cases. Proportional hazards assumptions were met. Survival curves are shown for all cancer sites combined as well as specific sites that showed statistically significant disparities by occupation. For sensitivity analyses, to assure enough follow-up period to detect survival differences across occupations, we performed the analyses among a restricted sample with a follow-up period for five years or more, which comprised 22849 women diagnosed with cancer between 1995-2003.

Patient or public involvement

No patient involved.

RESULTS

Table 1 summarizes the characteristics of female cancer cases used for analysis. Among a total of 61,110 cancer cases, 28.2% were diagnosed with cancer in their 40s.

Around half of the study sample were employed in Group 4 occupation (Blue-collar workers). During the follow-up period, 13,541 (22.2%) women died. Among them, 12552 (92.7%) died from cancer, 457 (3.4%) died from non-cancer and 532 (3.9%) had missing information on the cause of death. The most frequently diagnosed cancer sites were thyroid (25.0%), breast (20.7%), and stomach (11.3%). The cases of death were prevalent in stomach (2,453), breast (1,541), liver (1,483), lung (1,394) and colorectal cancer (1,315).

1 **Table 1. Characteristics of the study population**

		N	%
Total		61110	100.0
Age of diagnosis	<20	72	0.1
	20-29	5245	8.6
	30-39	15579	25.5
	40-49	17216	28.2
	50-59	15005	24.6
	60-	7993	13.1
Year of diagnosis	1995-1999	6654	10.9
	2000-2004	21861	35.8
	2005-2008	32595	53.3
Occupational group	Managers, professionals and technical workers	5822	9.5
	Clerks	15362	25.1
	Service and sales workers	7524	12.3
	Blue-collar workers	32402	53.0
Vital status	Alive	47569	77.8
	Dead	13541	22.2
		N (Death)	%
Cancer sites	Lip, oral cavity, and pharynx (C00-C14)	579 (143)	0.9
	Esophagus (C15)	59 (31)	0.1
	Stomach (C16)	6918 (2453)	11.3
	Colon, rectosigmoid junction, rectum (C18-C20)	4721 (1315)	7.7
	Liver and intrahepatic bile ducts (C22)	2026 (1483)	3.3
	Gallbladder, other and unspecified parts of biliary tract (C23-C24)	850 (562)	1.4
	Pancreas (C25)	605 (497)	1.0
	Larynx (C32)	33 (6)	0.1
	Trachea, bronchus, and lung (C33-C34)	2077 (1394)	3.4
	Mesothelioma (C45)	24 (17)	0.0
	Breast (C50)	12673 (1541)	20.7
	Cervix uteri (C53)	5271 (783)	8.6
	Corpus uteri (C54)	1416 (175)	2.3
	Ovary (C56)	1916 (557)	3.1
	Kidney (C64)	585 (104)	1.0
	Bladder (C67)	245 (39)	0.4
	Brain and other parts of central nervous system (C70-C72)	687 (339)	1.1

Thyroid gland (C73)	15295 (145)	25.0
Hodgkin lymphoma (C81)	79 (13)	0.1
Non-Hodgkin lymphoma (C82-C85, C96)	1209 (329)	2.0
Multiple myeloma (C90)	198 (112)	0.3
Leukemia (C91-C95)	1043 (591)	1.7

Hazard ratios (HRs) and 95% confidence intervals (CIs) of overall survival using managers, professionals and technical workers as the reference group are presented in Table 2.

1 **Table 2. Hazard ratios and their 95% Confidence intervals by occupational groups using Cox proportional hazard model**

		N	Death	Hazard Ratio*	95% Confidence interval
All cancer (C00-C97)	Managers, professionals and technical workers	5822	910	Reference	
	Clerks	15362	2186	**1.08**	**1.00 - 1.17**
	Service and sales workers	7524	1514	**1.25**	**1.15 - 1.35**
	Blue-collar workers	32402	8931	**1.34**	**1.25 - 1.44**
Stomach (C16)	Managers, professionals and technical workers	572	195	Reference	
	Clerks	1332	488	1.06	0.90 - 1.26
	Service and sales workers	816	307	1.16	0.97 - 1.39
	Blue-collar workers	4198	1463	1.09	0.94 - 1.28
Colorectal (C18-C20)	Managers, professionals and technical workers	328	88	Reference	
	Clerks	748	191	0.97	0.75 - 1.25
	Service and sales workers	500	129	0.97	0.74 - 1.28
	Blue-collar workers	3145	907	1.02	0.83 - 1.29
Liver (C22)	Managers, professionals and technical workers	110	72	Reference	
	Clerks	232	138	0.94	0.71 - 1.26
	Service and sales workers	223	151	1.08	0.82 - 1.44
	Blue-collar workers	1461	1122	1.23	0.98 - 1.58
Lung (C33-C34)	Managers, professionals and technical workers	148	89	Reference	
	Clerks	282	170	1.21	0.94 - 1.58
	Service and sales workers	218	136	1.15	0.88 - 1.50
	Blue-collar workers	1429	999	**1.41**	**1.14 - 1.77**
Breast (C50)	Managers, professionals and technical workers	1348	137	Reference	
	Clerks	3475	366	1.17	0.96 - 1.42
	Service and sales workers	1640	178	1.13	0.91 - 1.42
	Blue-collar workers	6210	860	**1.28**	**1.06 - 1.54**
Cervix uteri (C53)	Managers, professionals and technical workers	346	34	Reference	
	Clerks	831	84	1.21	0.82 - 1.82
	Service and sales workers	737	98	1.37	0.94 - 2.05
	Blue-collar workers	3357	567	**1.42**	**1.02 - 2.06**

Corpus uteri (C54)	Managers, professionals and technical workers	142	11	Reference	
	Clerks	295	27	1.56	0.79 - 3.29
	Service and sales workers	164	21	1.73	0.85 - 3.72
	Blue-collar workers	815	116	1.45	0.81 - 2.87
Ovary (C56)	Managers, professionals and technical workers	189	39	Reference	
	Clerks	547	101	0.92	0.64 - 1.35
	Service and sales workers	221	65	1.23	0.83 - 1.85
	Blue-collar workers	959	352	1.21	0.87 - 1.73
Thyroid (C73)	Managers, professionals and technical workers	1901	8	Reference	
	Clerks	5695	22	1.27	0.58 - 3.05
	Service and sales workers	1977	20	**2.22**	**1.02 - 5.36**
	Blue-collar workers	5722	95	**2.05**	**1.05 - 4.62**
Non-Hodgkin lymphoma (C82-C85, C96)	Managers, professionals and technical workers	133	21	Reference	
	Clerks	281	60	1.55	0.96 - 2.60
	Service and sales workers	151	40	1.58	0.94 - 2.73
	Blue-collar workers	644	208	**1.69**	**1.09 - 2.77**

* Adjusted by age and year of diagnosis

Blue-collar workers (HR 1.34, 95% CI 1.25-1.44) and service/sales workers (HR 1.25, 95% CI 1.15-1.35) showed poorer survival for all cancer sites combined compared to managers, professionals and technical workers. In terms of site-specific survival, blue-collar workers showed poorer survival for lung, breast, cervix uteri, and non-Hodgkin lymphoma, and both Blue-collar workers and service/sales workers showed significantly worse survival for thyroid cancer compared to managers, professionals and technical workers. Most other cancer sites (except for colorectal cancer) showed better survival for high SES occupation (managers, professionals and technical workers) as well, although the difference across occupational groups was not statistically significant.

Survival curves for all cancer combined and selected cancer sites by occupational groups are presented in Figure 2. For all sites combined, the survival rate was highest for managers, professionals and technical workers, followed by clerks, service and sales workers, and blue-collar workers, in that order. Women in blue-collar jobs exhibited an obviously less favorable survival pattern than managers, professionals and technical workers for lung cancer and non-Hodgkin lymphoma. Due to extremely high survival among thyroid cancer patients, absolute differences in survival across occupational groups were not found.

The sensitivity analyses with subgroups with follow-up period for 5 years or more showed a similar pattern, although they had a wider confidence interval due to decreased sample (Supplementary Table S1).

DISCUSSION

To our knowledge, this is the first Korean study to comprehensively document occupational disparities in overall survival in a female working population diagnosed with cancer.

Previous studies of cancer survival in Korea have looked at disparities based on educational attainment, medical insurance status, and area-level deprivation [15,17,19,20]. Studies focusing on occupational disparities in cancer survival have been mostly limited to western settings[21–23]. The hazard ratios for lower survival (comparing white collar workers to blue collar workers) are in a similar range to that found in our study, ranging from 1.0 to 1.4.

In the previous studies on socioeconomic cancer disparities, cancer of good prognosis showed a wider difference across SES groups[4,7,17]. Significant disparities in survival for breast, cervix uteri, thyroid cancer and non-Hodgkin lymphoma found in the present study are in line with those previous studies. Our findings are consistent with the "fundamental cause" theory of socioeconomic disparities advanced by Link and Phelan[24]. According to this theory, socioeconomic disparities in health arise due to differential access to and deployment of a variety of flexible resources to benefit health, including not only money and knowledge, but also symbolic prestige and powerful social connection by people with higher SES. Thus, it can be hypothesized that strong socioeconomic gradients in survival would be observed for cancer sites with a good prognosis, i.e., deaths which are highly preventable because effective modalities exist for early diagnosis and cure. On the other hand, fundamental cause theory predicts that SES disparities would be small or non-existent for cancers which have a uniformly poor prognosis and where effective screening is unavailable, where high SES people cannot utilize their resources.

Although lung cancer is often fatal for patients, it showed significant disparities as well in our data, showing a similar magnitude of difference across occupational groups with all cancer and cervix uteri cancer. As in other cancer sites, the main determinant of social disparities on lung cancer survival is known to be the stage at diagnosis and difference in treatment[25]. Medical cost for lung cancer was 3rd highest among all cancer sites in Korea [26]. Although Korea has universal health care system under National Health Insurance (NHI) or Medicaid program, patients still had to co-pay 20% of the cost of cancer treatment until 2005 (covered by our follow-up period), in which year the policy of decreasing cancer patients' co-payment to 10%. In a previous Korean study, utilization of inpatient and outpatient medical care of high-income cancer patients was more frequent than low-income patients, and the patients with higher incomes tend to use services from major tertiary hospitals[27]. Thus quality or differences in intensity of medical treatment could be a factor contributing to disparities in lung cancer survival[12].

Social disparities in cancer survival can be also attributed to differences in stage at diagnosis[13]. For the early detection of breast cancer and cervical cancer, the National Cancer Screening Program (NCSP) in Korea provides a mammogram and Pap smear every other year[28]. Despite the free access to screening, income and educational disparities in the uptake of screening continue to persist; the percentage of breast cancer screened population within the past two years were 36.2% in the lowest income group and 42.9% in the highest income group; and for cervical cancer, 43.2% and 65.1% respectively in 2005[29].

Besides NCSP, private health check-ups including cancer screening of which cost is paid fully by the examined individual have been prevalent in Korea. Many companies, usually larger than medium size, pay the fee of these check-ups for employees as a part of the well-fare system. According to a previous study, private cancer screening participation rate was higher in female office workers than in manual workers[30]. According to a previous Korean study, the lowest income group showed 1.35 times higher risk of advanced stage at the time of breast cancer diagnosis than the highest income group[31]. The difference in stage at diagnosis could explain our finding of significant disparities in the survival of breast and cervical cancer.

Factors other than socioeconomic circumstances could potentially contribute to occupational disparities in cancer survival, such as occupational exposure to carcinogens. For example, some studies reported an association between occupational exposure and site-specific survival in sinonasal cancer, bladder cancer, and non-Hodgkin lymphoma[32–34]. However, in a previous study on occupational disparities in cancer incidence, we did not find evidence of disparities in lung, bladder, or lympho-hematopoietic cancer in women[10]; thus, we believe that the impact of occupational exposures on survival disparities observed in the current study is likely to be limited.

The current study found the widest relative gap for overall survival in thyroid cancer across occupational groups. There has been a sharp rise in thyroid cancer incidence in Korea, attributed to screening and over-diagnosis[35]. Although survival was higher in high SES occupations with thyroid cancer, the incidence was also significantly higher in the same occupational group in the previous study with the same data source[10]. Generally, thyroid cancer survival in Korean women is extremely high, more than 98% 5-year survival rate since 2001[1]. Indeed, the absolute differences between occupational groups during the follow-up period were not observable in survival curves due to extremely low mortality across all occupational groups. Considering the clear opposite trend of the occupational gradient in incidence and survival, and the very low mortality, the finding of survival disparities in thyroid cancer might be partly due to over-diagnosis which first started among high SES women.

Although clinical factors such as stage at diagnosis and treatment are observed as the most important determinants of cancer survival social disparities, a number of studies found persistent SES disparities in survival even after adjusting for stage and treatment[12]. Psychosocial factors associated with SES are also considered to play a role in cancer survival, e.g. the impact of social support on breast cancer survival[36].

Our findings with regards to occupational disparities on overall survival in women with cancer (all sites combined) are in line with previous findings in men in Korea; HR 1.38, 95% CI 1.33-1.43 for service/sales workers, HR 1.45, 95% CI 1.42-1.48 for blue-collar workers[7]. There was no obvious difference between men and women on risk estimates in survival disparity in all cancer, although men had more cancer sites with statistically significant results. By contrast, occupational disparities in cancer incidence or mortality are more substantial in men than in women according to previous Korean studies[10,11]. These findings would seem to suggest that factors related to cancer survival, such as earlier detection and better treatment can be more important factors than factors related to cancer incidence - health behavior (i.e., smoking and alcohol) or occupational carcinogen exposure - for reducing cancer disparities among working women in Korea.

The present study had some strengths. First, using a large and representative workers cohort and cancer registry data enabled us to analyze a number of specific cancer sites with a sufficient number of cases. The database used for this study, the Employment Insurance data and the National Cancer registry are very complete; therefore, the findings of this study are generalizable to the population of working women in Korea. Second, due to our longitudinal follow-up design, we included only incident cases; hence, reverse causation (i.e. cancer diagnosis resulting in a change in occupation) can be ruled out. Third, we classified occupations based on the information from the Employment Insurance data, which is determined by the companies hiring the individuals. This information is expected to be more accurate than the information collected by self-report.

This study also has several limitations. First, due to the lack of information on important covariates including a stage at diagnosis, treatment information, we could not evaluate the contribution of mediating variables between occupation and survival. Second, the occupational information was available only for 1995-2000; therefore we could not consider the change of occupation after 2000. Also, the workers' data to match cancer registry were available for only the workers who held the same occupation between 1995 and 2000, hence the women who diagnosed with cancer before 2000 could not be selected in the study if they had changed occupation between cancer diagnosis and 2000. However, around 90% of study sample was diagnosed with cancer after 2000, and they were included in the analysis regardless of changing occupation after cancer diagnosis.

Our study sample did not include women who were not in paid employment. Female labor force participation rates were between 47.0-49.5% for all ages in Korea during 1995-2000, the period covered by our data[37]. Thus, the results are not generalizable to all women in Korea. Furthermore, unemployed women and homemakers showed lower participation in cancer screening than employed women according to a previous study[30]. Overall survival differences among cancer patients might be wider in the general population if we include unemployed women.

Even though we used large registry data, we did not perform subgroup analysis for rare cancer due to a small number of cases. Among the analyzed cancer sites, corpus uteri and thyroid cancer showed relatively wide confidence interval due to smaller number of patients or deaths.

In conclusion, we found substantial occupational disparities in overall survival among Korean working women with cancer, particularly in lung, breast, thyroid cancer, and non-

Hodgkin lymphoma. Further investigation to assess the influence of possible mediators between occupation and cancer survival is warranted. Health policies should enhance access to cancer screening and quality of treatment among cancer patients with lower SES occupations.

Contributors HEL and EAK conceived of the presented idea. HEL designed the study and performed statistical analysis. IK, EAK and MZ participated in its design. HEL wrote the first draft of the manuscript. EAK, MZ and IK critically revised the manuscript. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by the institutional review boards of the Occupational Safety and Health Research Institute and Korea Occupational Safety and Health Agency (KOSHA), Ulsan, Korea. Approval no: COD-89.

Data availability statement The data using this study was obtained by combining the national cancer registry, death statistics, and Korean Employment Insurance system during the governmental investigation projects, which cannot be in public.

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Figure Legends

Figure 1 Selection of study population

Figure 2 Survival curves by occupational groups and selected cancer sites

Adjusted by age and year of diagnosis

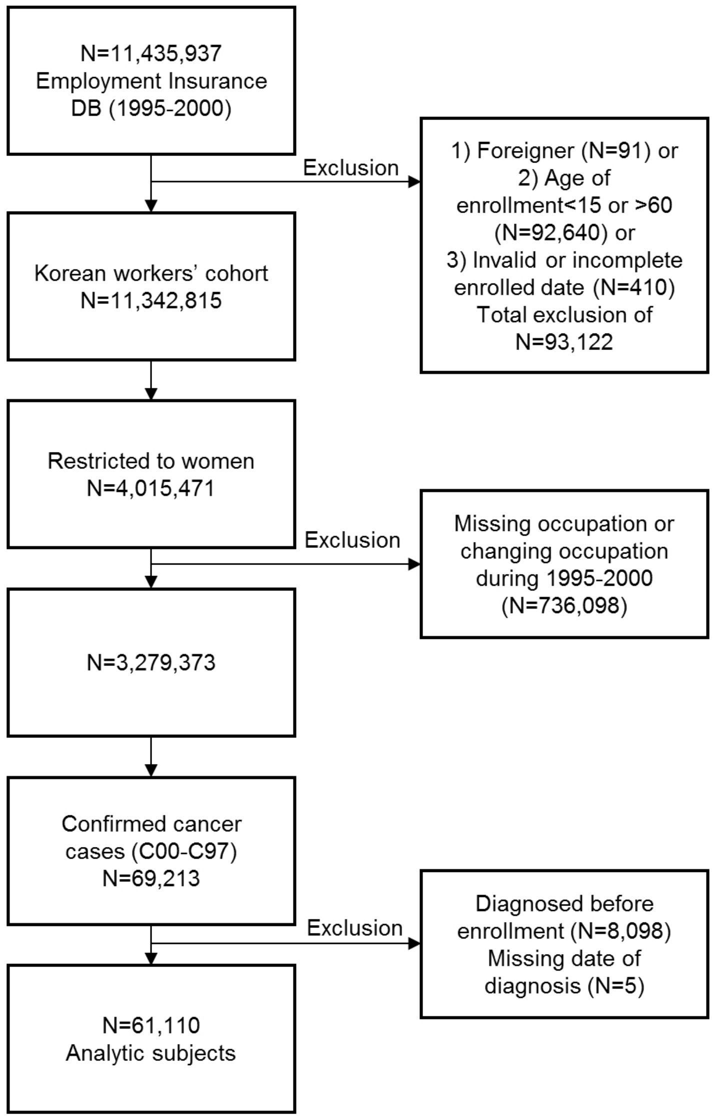

Figure 1 Selection of study population

85x129mm (300 x 300 DPI)

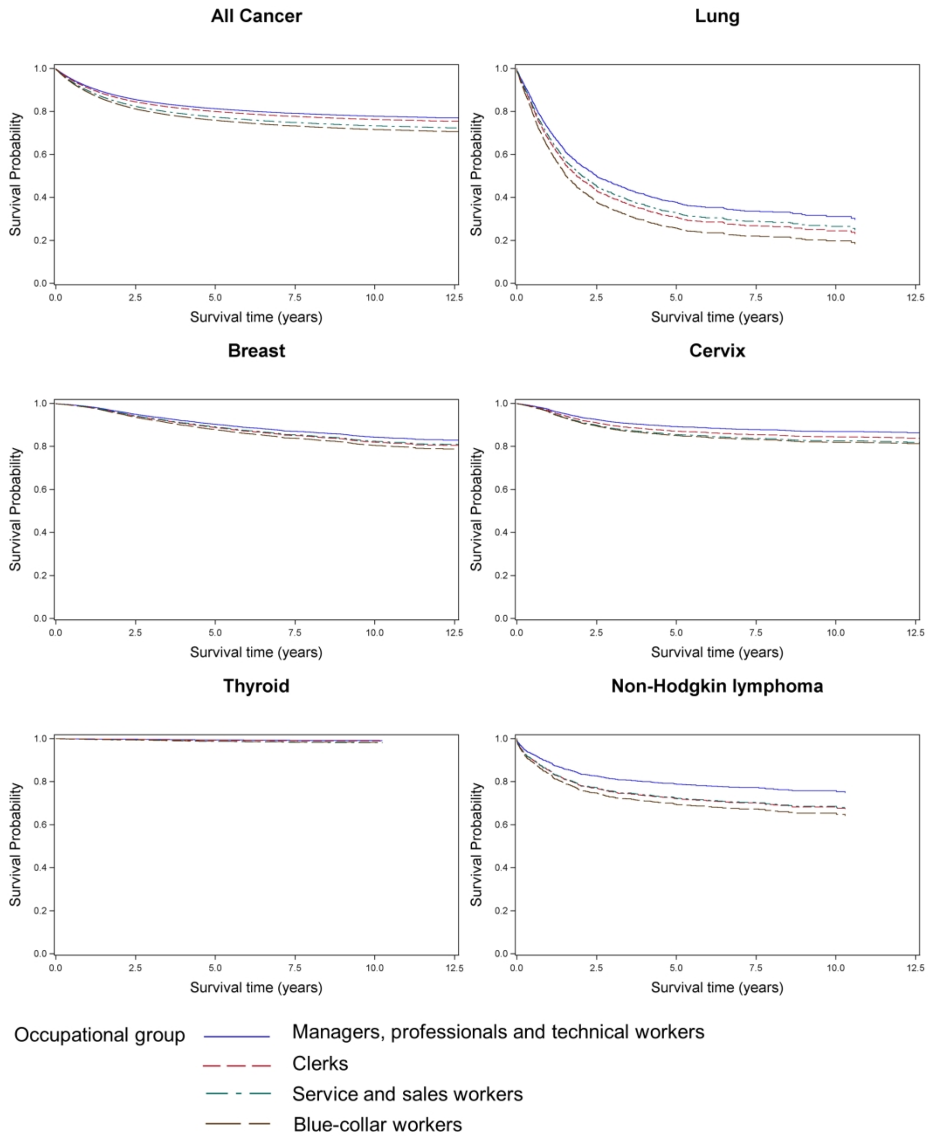

Figure 2 Survival curves by occupational groups and selected cancer sites
Adjusted by age and year of diagnosis

175x224mm (300 x 300 DPI)

Supplementary Table S1. Hazard ratios and their 95% Confidence intervals by occupational groups using Cox proportional hazard model in sensitivity analysis restricted to women followed up for 5 years or more

		N	Death	Hazard Ratio*	95% Confidence interval	
All cancer (C00-C97)	Managers, professionals and technical workers	1981	497	Reference		
	Clerks	4814	1194	1.11	1.00	1.24
	Service and sales workers	2646	835	**1.28**	**1.14**	**1.43**
	Blue-collar workers	13408	5098	**1.34**	**1.23**	**1.48**
Stomach (C16)	Managers, professionals and technical workers	230	101	Reference		
	Clerks	541	268	1.12	0.89	1.42
	Service and sales workers	332	165	1.22	0.96	1.57
	Blue-collar workers	1968	891	1.16	0.94	1.44
Colorectal (C18-C20)	Managers, professionals and technical workers	110	43	Reference		
	Clerks	246	102	1.03	0.73	1.49
	Service and sales workers	157	59	0.98	0.67	1.47
	Blue-collar workers	1213	503	1.11	0.82	1.55
Liver (C22)	Managers, professionals and technical workers	50	36	Reference		
	Clerks	101	65	0.92	0.61	1.39
	Service and sales workers	101	86	1.36	0.93	2.03
	Blue-collar workers	674	586	**1.42**	**1.03**	**2.03**
Lung (C33-C34)	Managers, professionals and technical workers	55	45	Reference		
	Clerks	102	78	1.13	0.78	1.65
	Service and sales workers	86	72	1.16	0.81	1.70
	Blue-collar workers	560	475	1.31	0.97	1.80
Breast (C50)	Managers, professionals and technical workers	511	91	Reference		
	Clerks	1119	209	1.10	0.86	1.41
	Service and sales workers	576	106	1.09	0.82	1.44
	Blue-collar workers	2688	610	**1.30**	**1.05**	**1.64**
Cervix uteri (C53)	Managers, professionals and technical workers	179	23	Reference		
	Clerks	345	52	1.28	0.79	2.12
	Service and sales workers	359	61	1.30	0.82	2.15
	Blue-collar workers	1964	384	1.28	0.86	2.01
Corpus uteri (C54)	Managers, professionals and technical workers	58	5	Reference		
	Clerks	105	13	2.00	0.74	6.29
	Service and sales workers	53	10	2.09	0.74	6.73
	Blue-collar workers	324	65	1.89	0.84	5.41
Ovary (C56)	Managers, professionals and technical workers	93	24	Reference		
	Clerks	267	47	0.68	0.42	1.13
	Service and sales workers	97	31	0.96	0.56	1.65

	Blue-collar workers	478	231	1.16	0.77	1.85
Thyroid (C73)	Managers, professionals and technical workers	369	3	Reference		
	Clerks	1113	7	1.19	0.33	5.53
	Service and sales workers	417	14	**4.22**	**1.38**	**18.31**
	Blue-collar workers	1289	50	2.27	0.82	9.40
Non-Hodgkin lymphoma (C82-C85, C96)	Managers, professionals and technical workers	53	12	Reference		
	Clerks	101	36	1.73	0.93	3.48
	Service and sales workers	64	13	0.76	0.34	1.69
	Blue-collar workers	283	114	1.54	0.86	3.01

*Adjusted by age and year of diagnosis

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, explain how loss to follow-up was addressed	8
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	Fig1
		(c) Consider use of a flow diagram	Fig1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	10
		(c) Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	Report numbers of outcome events or summary measures over time	8

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table2
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Fig2
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.