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Article

Occupational inequalities in female cancer incidence in Japan: Hospital-based matched case-control study with occupational class

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ABSTRACT

Background: Socioeconomic inequalities in female cancer incidence have previously been undocumented in Japan.

Methods: Using a nationwide inpatient dataset (1984–2016) in Japan, we identified 143,806 female cancer cases and 703,157 controls matched for sex, age, admission date, and admitting hospital, and performed a hospital-based matched case-control study. Based on standardized national classification, we categorized patients' socioeconomic status (SES) by occupational class (blue-collar, service, professional, manager), cross-classified by industry sector (blue-collar, service, white-collar). Using blue-collar workers in blue-collar industries as the reference group, we estimated the odds ratio (OR) for each cancer incidence using conditional logistic regression with multiple imputation, adjusted for major modifiable risk factors (smoking, alcohol consumption).

Results: We identified lower risks among higher-SES women for common and overall cancers: e.g., ORs for managers in blue-collar industries were 0.67 (95% confidence interval [CI], 0.46–0.98) for stomach cancer and 0.40 (95% CI, 0.19–0.86) for lung cancer. Higher risks with higher SES were evident for breast cancer: the OR for professionals in service industries was 1.60 (95% CI, 1.29–1.98). With some cancers, homemakers showed a similar trend to subjects with higher SES; however, the magnitude of the OR was weaker than those with higher SES.

Conclusions: Even after controlling for major modifiable risk factors, socioeconomic inequalities were evident for female cancer incidence in Japan.

1. Background

Socioeconomic status (SES), including occupational class, has been recognized as a fundamental social determinant of health, and that also applies to cancer incidence (Krieger et al., 1999). Among women in Western countries, evidence suggests that the risks of upper digestive cancer (e.g., stomach cancer) and lung cancer show an inverse socioeconomic gradient (i.e., a reduced cancer risk with higher SES) (Faggiano, Partanen, Kogevinas, & Boffetta, 1997). The fundamental cause theory of SES and health—developed by Link and Phelan in 1995—argues that the robust association between SES and health arises because SES "embodies an array of resources, such as money, knowledge, prestige, power, and beneficial social connections that protect health no matter what mechanisms are relevant at any given time." (Link & Phelan, 1995) For example, the connection between SES and stomach cancer and lung cancer can be explained by socioeconomic disparities in smoking, alcohol drinking, and other health behaviors (Faggiano et al., 1997; Krieger et al., 1999; Uthman, Jadidi, & Moradi, 2013; Weiderpass & Pukkala, 2006).

However, higher SES does not protect against the risk of cancer in every instance. For example, breast cancer tends to show a positive socioeconomic gradient (i.e., an excess cancer risk with higher SES). That finding has been attributed to socioeconomic differences in reproductive behavior, e.g., overall fertility, age at first birth, and spacing of births (Faggiano et al., 1997; Larsen et al., 2011). Thus, it would be more accurate to state that higher SES tends to be associated with better (overall) health irrespective of the relevant mechanisms at any given time; however, *specific* health outcomes (e.g., breast cancer) can be positively correlated with high SES depending on the background context.

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To our knowledge, although some studies on the socioeconomic gradient in cancer *mortality* (though not cancer incidence) are available (Eguchi, Wada, Prieto-Merino, & Smith, 2017; Tanaka et al., 2017), the documentation of socioeconomic inequalities in female cancer incidence remains sparse in Asian countries, including Japan. Sex differences exist in the etiology of cancer (e.g., frequency, pathology, and survival) (Hori et al., 2015; Zaitsu et al., 2015), and the distribution of higher SES (professionals and managers) in women is different from that in men in Japan (Tanaka et al., 2017). In addition, the risk associated with homemakers has not yet been identified. Therefore, it is necessary to determine the socioeconomic disparities in female cancer incidence in Japan separately from those with males.

Using a nationwide inpatient dataset that included details of occupational class (with homemakers as a separate category) as a proxy for SES (Mannetje & Kromhout, 2003), we examined whether a socioeconomic gradient was associated with the risks for overall and site-specific cancer incidence among women in Japan. We also determined whether any observed socioeconomic gradient remained even after controlling for mediation by major modifiable behavioral factors (smoking and alcohol consumption).

2. Methods

2.1. Study setting

We conducted a hospital-based matched case-control study using female patient data (1984–2016) from the nationwide clinical and occupational database of the Rosai Hospital group, run by the Japan Organization of Occupational Health and Safety (JOHAS), an independent administrative agency. Details of the database have been described elsewhere (Kaneko, Kubo, & Sato, 2015; Zaitsu, Kawachi, Takeuchi, & Kobayashi, 2017; Zaitsu et al., 2016). Briefly, the Rosai Hospital group consists of 34 general hospitals in major urban areas of Japan; it has collected medical chart information (including basic sociodemographic characteristics, clinical history and diagnosis, pathological information, treatment, and outcomes for every inpatient) since 1984. The clinical diagnosis, extracted from physicians' medical charts confirmed at discharge, is coded according to the International Classification of Diseases and Related Health Problems, 9th Revision (ICD-9) or 10th Revision (ICD-10) (Kaneko et al., 2015; Zaitsu et al., 2016, 2017). From questionnaires completed at the time of admission, the database includes the occupational history of each inpatient (current and three most recent jobs, including the age of starting and ending) as well as smoking and alcohol habits. The detailed occupational history is coded using the standardized three-digit codes of the Japan Standard Occupational Classification and Japan Standard Industrial Classification; they correspond, respectively, to the International Standard Industrial Classification and International Standard Occupational Classification (Kaneko et al., 2015; Zaitsu et al., 2016, 2017). According to the revisions of the Japan Standard Occupational Classification and Japan Standard Industrial Classification during the study period, JOHAS updated the previous job codes to be consistent with changes in coding practice (Zaitsu et al., 2016). Written informed consent was obtained before patients completed the questionnaires; trained registrars and nurses are responsible for registering the data. The database currently contains details from over 6 million inpatients.

2.2. Cases and controls

The study subjects comprised 846,963 female patients (143,806 cancer cases, 703,157 hospital controls) aged 20 years or older admitted to hospital between 1984 and 2016. Controls for each cancer case were matched by sex, age (same 5-year age category), admission date (same financial year), and hospital (Zaitsu et al., 2016). We randomly sampled five controls for each cancer case; however, the matching process generated fewer than five controls for some cancer cases. The matched background characteristics (age, admission date, and admitting hospital) were well balanced between the cases and controls: e.g., mean age of the cases and controls was, respectively, 65 years (SD 14.5 years) and 64 years (SD 14.4 years).

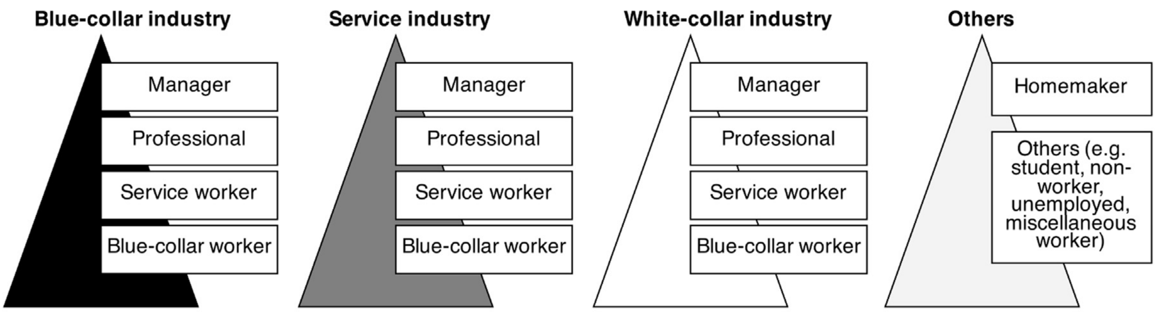
The cancer cases were those patients whose main diagnoses were cancer, confirmed by physicians on discharge, for the first-time stay in the hospitals for the initial cancer, together with pathological or imaging information (e.g., computed tomography, magnetic resonance imaging, and endoscopy); they did not have a previous history of malignant disease (Zaitsu et al., 2016, 2017). We defined cancer incidence by the diagnosis of cancer cases; the validation for the diagnosis corresponding to ICD-9 or ICD-10 in the database has been described elsewhere (Kaneko et al., 2015; Zaitsu et al., 2016, 2017). The database is unique to the Rosai Hospital group and so differs from medical claims data, which may have less diagnostic accuracy (Sato, Yagata, & Ohashi, 2015). Following national statistics for Japan (Hori et al., 2015), we specified the top 10 common female cancer sites: breast (17.4%); colon and rectum (13.8%); stomach (13.8%); lung (5.7%); liver (4.7%); pancreas (2.9%); gallbladder (2.2%); malignant lymphoma (3.3%); cervix (4.8%); and uterus (3.1%; Supplementary Table 1). Less common cancers (from 14 sites) were additionally specified. The prevalence of these cancers was almost identical to that in national statistics (Supplementary Table 1) (Hori et al., 2015). The total of female cancer cases in the present study amounted to 1.9% of the total expected female cancer cases in Japan for the years 1984–2013 (134,767 of 6,925,517) (Hori et al., 2015).

Our control subjects comprised female patients who were admitted to hospital with a diagnosis of the following: eye or ear diseases (ICD-9, 360–389 and ICD-10, H00–H95; 37.0%); genitourinary system diseases (ICD-9, 580–629 and ICD-10, N00–N99; 24.4%); infectious or parasitic diseases (ICD-9, 1–136 and ICD-10, A00–B99; 10.7%); skin diseases (ICD-9, 680–709 and ICD-10, L00–L99; 5.1%); symptoms and abnormal findings, such as dizziness and chest and abdominal pain (ICD-9, 780–799 and ICD-10, R00–R99; 9.4%); or other diseases, such as congenital malformation (ICD-9, 280–289, 740–779, and ICD-10, D50–D77, P00–P96, Q00–Q99; 13.4%) (Zaitsu et al., 2016, 2017). Estimating odds for each control disease against the rest of the other five control diseases in a prior analysis within 124,087 control subjects, we assumed that these diagnoses selected for the control group were not linked to SES (Supplementary Fig. 1).

2.3. SES grouped by occupation and industry combination and other covariates

We selected the longest-held job for each patient from her occupational history to categorize SES. Owing to the enormous variety of occupations in the dataset, we aggregated the longest-held occupational class into four major occupational groupings (Galobardes, Shaw, Lawlor, Lynch, & Davey Smith, 2006; Mannetje & Kromhout, 2003; Tanaka et al., 2017): blue-collar workers, service workers, professionals, and managers. We additionally cross-classified the longest-held occupations into three industrial sectors (Jackson, Redline, Kawachi, Williams, & Hu, 2013; Mannetje & Kromhout, 2003; Tanaka et al., 2017): blue-collar industry, service industry, and white-collar industry (Fig. 1). Further, within the "others" group (comprising homemakers, students, non-workers, unemployed, and miscellaneous workers) (Zaitsu et al., 2018), we distinguished between homemakers and the remainder (Fig. 1). The major profile of SES among the study subjects did not largely differ from that in national statistics (Supplementary Table 2). The average length of the longest held jobs was 27 years.

Age, admission date, and admitting hospital were confounding factors (Zaitsu et al., 2016, 2017). The major modifiable behavioral factors, i.e., smoking (pack-years) and alcohol consumption (daily amount), were mediating factors (Zaitsu et al., 2016, 2017).



Occupational class	Japan Standard Occupational Classification	2-digit code
Blue-collar worker	Security, agriculture, forestry, fishery, manufacturing, transport and machine operation (stationary and construction machinery operators, construction, mining, carrying, cleaning, packaging, and related workers)	43–59, 64–73
Service worker	Clerical, sales, service, and transport and machine operation (railway drivers, motor vehicle drivers, ship and aircraft operators, and other transport related workers)	25–42, 60–63
Professional	Professional and engineering workers	05–24
Manager	Administrative and managerial workers	01–04
Industrial cluster	**Japan Standard Industrial Classification**	**Major code**
Blue-collar industry*	Agriculture, forestry, fisheries, mining, quarrying of stone, construction, manufacturing, electricity, gas, heat supply, water, transport, and postal service	A–F, H
Service industry	Wholesale, retail trade, accommodations, eating, drinking, living-related, personal, amusement, and compound services, services not elsewhere categorized	I, M, N, Q, R
White-collar industry†	Information, communications, finance, insurance, real estate, goods rental, leasing, education, learning support, medical, healthcare, welfare, and government except elsewhere classified	G, J, K, L, O, P, S

* Waste disposal business (Code R88) included. † Political, business and cultural organizations (Code R93), railway transport (Code H42), road passenger transport (Code H43), and air transport (Code H46) included.

Fig. 1. Socioeconomic status grouped by longest-held occupational class cross-classified with industrial cluster.

2.4. Statistical analysis

We performed multiple imputation for missing data among the 846,963 study subjects using all data, including SES, smoking, and alcohol consumption; five imputed datasets were generated (Zaitsu, Kawachi, Ashida, Kondo, & Kondo, 2018). The following missing data were multiply imputed: SES (285,737, 33.7%), smoking (267,392, 31.6%), and alcohol consumption (346,150, 40.9%). The basic demographics (i.e., age, admission date, and admitting hospital) were similar between those with complete and incomplete data for SES; however, some lifestyle habits such as smoking and drinking differed between those with complete and incomplete data. Excluding incomplete data may lead to biased inference; therefore, we conducted multiple imputation analysis (Supplementary Table 3).

Using blue-collar workers in blue-collar industries as the referent category, we estimated odds ratios (ORs) and 95% confidence intervals (CIs) in each SES for each specific cancer site as well as overall cancer incidence. For primary analysis to assess baseline socioeconomic gradients in female cancer incidence, we used conditional logistic regression with multiple imputation matched for age, admission date, and admitting hospital (model 1) (Zaitsu et al., 2016, 2018). The five ORs and 95% CIs obtained at each imputed dataset were combined into one combined OR and 95% CI. To assess the contribution of major modifiable behavioral factors, we additionally adjusted for smoking and alcohol consumption as mediation factors (model 2).

For sensitivity analysis, we restricted the analysis to never smokers (82,969 cases, 341,792 controls). Owing to the insufficient number of the cases for less common types, we limited the analysis to overall and the top 10 common cancers. Additionally, we performed conditional logistic regression for patients with complete information (84,848 cases, 396,677 controls) without performing multiple imputation. For Supplementary data analysis using an alternative control group (all available controls with all benign diseases matched for age, diagnostic data, and admitting hospital), we performed conditional logistic regression with multiple imputation for stomach cancer (19,840 cases, 99,160 controls) and breast cancer (24,983 cases, 124,905 controls). Alpha was set at 0.05, and all *P* values were two-sided. Data were analyzed using STATA/MP13.1 (Stata-Corp LP, College Station, TX).

3. Results

Among the top 10 common female cancers in Japan, we observed an inverse socioeconomic gradient (i.e., reduced risk with higher SES) for stomach and lung cancers (Fig. 2). In blue- and white-collar industries, higher SES (professionals and managers) had lower odds for stomach cancer (the OR ranged from 0.68 for managers in blue-collar industries to 0.77 for professionals in white-collar industries) and lung cancer (OR 0.47 for managers in blue-collar industries; Table 1). Even after fully controlling for smoking and alcohol consumption, the observed lower odds in higher SES were not attenuated; they remained significantly associated with stomach cancer (adjusted OR ranged from 0.67 for managers in blue-collar industries to 0.78 for professionals in white-collar industries) and lung cancer (adjusted OR 0.40 for managers in blue-collar industries, model 2, Table 1). Homemakers showed a similar trend to subjects with higher SES (Fig. 2); however, the magnitude of the OR was weaker than those with higher SES (adjusted OR, 0.80 for

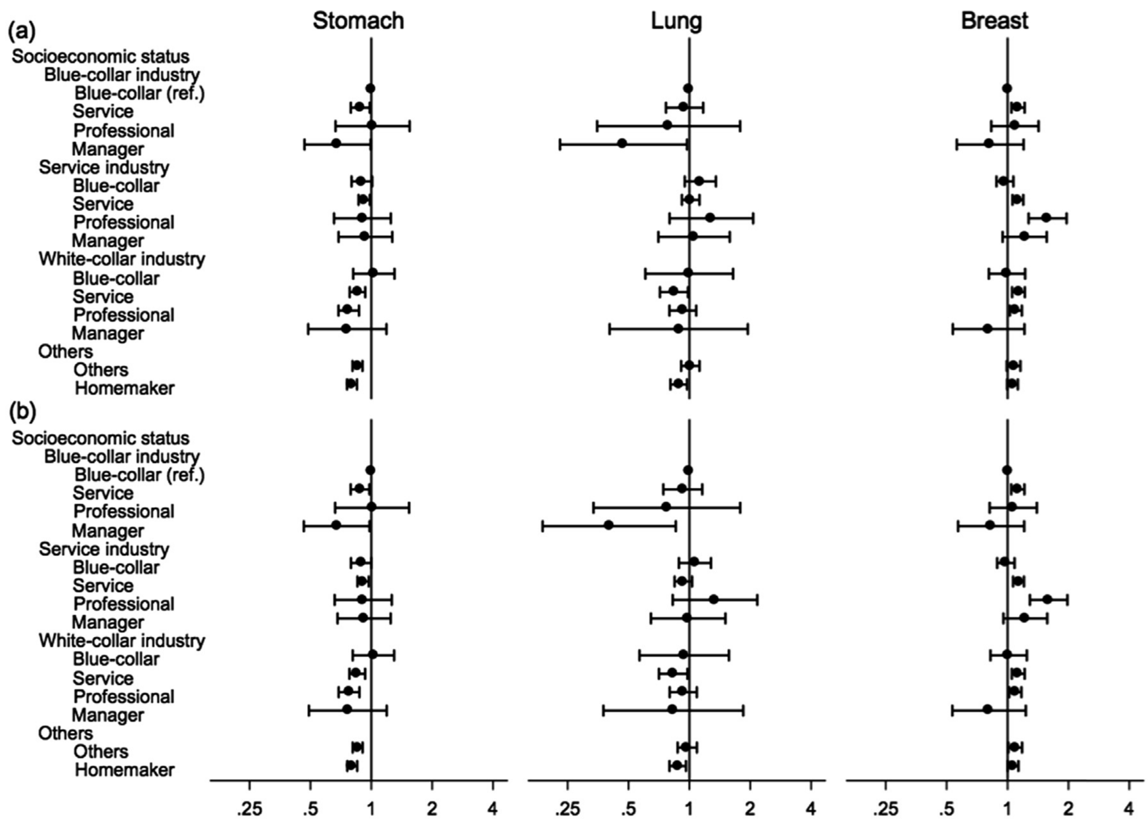


Fig. 2. Socioeconomic gradients associated with risk for incidence of stomach, lung, and breast cancers. The odds ratio (dot) and 95% confidence interval (bar) were estimated by conditional logistic regression, (a) matched for age, admission date, and admitting hospital and (b) additionally adjusted for smoking and alcohol consumption, with five imputed datasets. The numbers of cases and controls used for analysis were, respectively, 19,840 and 96,658 for stomach cancer, 8,207 and 39,941 for lung cancer, and 24,983 and 122,414 for breast cancer.

stomach cancer and 0.87 for lung cancer, model 2, Table 1).

By contrast, we found a positive socioeconomic gradient (i.e., excess risk with higher SES) for breast cancer (Fig. 2). In service and white-collar industries, higher SES showed higher odds for breast cancer (OR ranged from 1.10 for professionals in white-collar industries to 1.58 for professionals in service industries; Table 2). Even after fully controlling for smoking and alcohol consumption, the observed higher odds with higher SES were not attenuated and remained significantly associated with breast cancer (adjusted OR ranged from 1.09 for professionals in white-collar industries to 1.60 for professionals in service industries, model 2, Table 2). The risk for homemakers (as well as service workers in all industries) was again similar to subjects with higher SES (Fig. 2); however, the magnitude of the OR was weaker than those with higher SES (adjusted ORs ranged from 1.06 for homemakers to 1.13 for service workers in service and white-collar industries, model 2, Table 2).

Among the remainder of common cancers, we observed no socioeconomic gradient (i.e., reduced or excess risk with higher SES); however, pancreatic, gallbladder, malignant lymphoma, and cervical cancer appeared to hint at a possible inverse gradient pattern (Supplementary Fig. 2, Supplementary Table 4). The overall cancer incidence showed a weak inverse socioeconomic gradient (Fig. 3), which persisted even after fully controlling for smoking and alcohol consumption (adjusted OR ranged from 0.84 for managers in white-collar industries to 0.91 for professionals in white-collar industries, model 2, Table 2).

Less common cancers did not show a socioeconomic gradient (Supplementary Fig. 3); however, certain cancers (e.g., those of the oral cavity, pharynx, and esophagus) appeared to show a possible inverse gradient pattern (Supplementary Table 4). In the sensitivity analysis, although the precise odds estimated with various regression analyses differed according to the analytic model and analyzed population, the direction of the socioeconomic gradient was almost identical (Supplementary Figs. 4 and 5). Likewise, the results from the alternative control group (i.e., all benign diseases) showed the same socioeconomic gradient pattern (Supplementary Fig. 6). In addition, smoking and alcohol consumption were independently associated with most of the risk for site-specific and overall cancer incidence, regardless of SES (Supplementary Table 5 and 6).

4. Discussion

4.1. All cancer sites

Studies in Western countries suggest a slightly inverse socioeconomic gradient in such nations as Finland; in some instances, there is a fairly flat gradient for overall female cancer incidence in Denmark, Sweden, and France (Faggiano et al., 1997; Melchior et al., 2005). With the Japanese data in the present study, we found a weak inverse overall socioeconomic gradient; this result suggests that the inverse socioeconomic gradients for stomach and lung cancers (which made up approximately 20% of all incident cancers) were partially canceled by the positive socioeconomic gradient for breast cancer (accounting for 18% of all incident cancer).

4.2. Stomach cancer

An inverse socioeconomic gradient for stomach cancer has been consistently reported in Western countries (Faggiano et al., 1997; Spadea et al., 2010; Weiderpass & Pukkala, 2006). A recent systematic review reached the same conclusion (Uthman et al., 2013). This pattern may be partly due to less smoking and drinking with higher SES (Uthman et al., 2013; Weiderpass & Pukkala, 2006). However, in the present study, an inverse socioeconomic gradient persisted after

Table 1
Odds ratios for each socioeconomic status associated with risk for female stomach and lung cancer incidence.

		Control, %	Case, %	Model 1[a]		Model 2[b]	
				OR (95% CI)	*P*	OR (95% CI)	*P*
Stomach							
n		96,658	19,840				
SES							
Blue-collar industry	Blue-collar worker	16.9	19.3	1.00		1.00	
	Service worker	3.7	3.7	0.88 (0.79–0.98)	.02	0.88 (0.79–0.98)	.02
	Professional	0.2	0.2	1.01 (0.67–1.55)	.94	1.01 (0.66–1.54)	.97
	Manager	0.4	0.3	0.68 (0.47–0.99)	.05	0.67 (0.46–0.98)	.04
Service industry	Blue-collar worker	2.5	2.6	0.90 (0.80–1.01)	.07	0.89 (0.79–1.00)	.05
	Service worker	12.8	13.5	0.92 (0.86–0.98)	.01	0.91 (0.85–0.97)	.005
	Professional	0.2	0.2	0.90 (0.65–1.25)	.54	0.91 (0.66–1.26)	.58
	Manager	0.4	0.5	0.94 (0.69–1.27)	.66	0.92 (0.68–1.25)	.58
White-collar industry	Blue-collar worker	0.4	0.5	1.03 (0.81–1.30)	.81	1.02 (0.81–1.30)	.84
	Service worker	4.7	4.6	0.85 (0.78–0.93)	< .001	0.85 (0.78–0.93)	< .001
	Professional	4.8	4.3	0.77 (0.69–0.87)	< .001	0.78 (0.69–0.87)	< .001
	Manager	0.2	0.2	0.76 (0.49–1.19)	.22	0.76 (0.49–1.19)	.23
Others	Others	20.2	20.0	0.85 (0.81–0.90)	< .001	0.86 (0.81–0.91)	< .001
	Homemaker	32.6	30.3	0.80 (0.76–0.85)	< .001	0.80 (0.76–0.85)	< .001
Smoking							
	Never	73.7	73.6			1.00	
	≤ 20 pack-year	22.5	21.2			0.95 (0.89–1.00)	.07
	> 20–40 pack-year	2.9	3.9			1.31 (1.20–1.43)	< .001
	> 40 pack-year	0.8	1.4			1.59 (1.38–1.84)	< .001
Alcohol consumption							
	Never	70.5	71.2			1.00	
	≤ 15 g/day	17.7	15.9			0.89 (0.85–0.95)	< .001
	> 15–30 g/day	10.1	10.6			1.02 (0.96–1.09)	.50
	> 30 g/day	1.8	2.3			1.17 (1.02–1.34)	.02
Lung							
n		39,941	8,207				
SES							
Blue-collar industry	Blue-collar worker	15.4	16.2	1.00		1.00	
	Service worker	3.7	3.6	0.95 (0.77–1.17)	.59	0.93 (0.74–1.16)	.48
	Professional	0.1	0.1	0.79 (0.35–1.78)	.56	0.77 (0.34–1.78)	.54
	Manager	0.4	0.2	0.47 (0.23–0.97)	.04	0.40 (0.19–0.86)	.02
Service industry	Blue-collar worker	2.5	3.0	1.13 (0.95–1.35)	.17	1.07 (0.89–1.28)	.49
	Service worker	12.6	13.4	1.01 (0.92–1.12)	.77	0.93 (0.84–1.03)	.17
	Professional	0.2	0.3	1.28 (0.80–2.07)	.30	1.34 (0.83–2.17)	.24
	Manager	0.4	0.5	1.05 (0.70–1.58)	.80	0.99 (0.65–1.51)	.95
White-collar industry	Blue-collar worker	0.4	0.4	1.00 (0.61–1.65)	.99	0.94 (0.57–1.57)	.81
	Service worker	4.5	4.0	0.84 (0.72–0.98)	.03	0.83 (0.71–0.98)	.03
	Professional	4.5	4.3	0.93 (0.80–1.08)	.33	0.93 (0.80–1.09)	.37
	Manager	0.2	0.2	0.89 (0.40–1.95)	.75	0.83 (0.38–1.84)	.63
Others	Others	18.8	20.1	1.01 (0.91–1.12)	.85	0.98 (0.87–1.09)	.65
	Homemaker	36.2	33.7	0.89 (0.81–0.97)	.01	0.87 (0.80–0.96)	.006
Smoking							
	Never	72.8	64.0			1.00	
	≤ 20 pack-year	22.9	23.2			1.23 (1.13–1.33)	< .001
	> 20–40 pack-year	3.2	7.9			2.98 (2.68–3.32)	< .001
	> 40 pack-year	1.0	4.9			5.76 (4.94–6.71)	< .001
Alcohol consumption							
	Never	68.7	68.4			1.00	
	≤ 15 g/day	18.4	16.2			0.81 (0.71–0.92)	.004
	> 15–30 g/day	11.0	12.2			0.92 (0.80–1.05)	.19
	> 30 g/day	1.9	3.2			0.96 (0.79–1.17)	.70

[‡]Data were estimated with five imputed datasets. Percentages may not total 100 because of rounding with multiple imputation. OR, odds ratio; CI, confidence interval; SES, socioeconomic status.

[a] Conditional logistic regression matched for age, admission date, and admitting hospital.

[b] Additional adjustment for smoking and alcohol consumption.

controlling for potential mediation by smoking and drinking. Other factors may therefore play a role.

In Japan, dietary habits (e.g., higher consumption of salty food with lower SES associated with the risk of stomach cancer) could be a potential explanation (Miyaki et al., 2013; Umesawa et al., 2016). *Helicobacter pylori* infection is an additional explanation: the probability of infection in childhood is likely to be lower among individuals with high SES than in those with low SES (Uthman et al., 2013). However, *H. pylori* infection was not a predictor of the incidence of stomach cancer among women in the Hisayama cohort in Japan (but it was a predictor for men); that is partially because of the high prevalence of *H. pylori* infection (approximately 63%) and potential uncontrolled confounders, such as SES (Yamagata et al., 2000).

To some extent in Japan, national cancer screening is associated with the prevention of stomach cancer (Leung et al., 2008). With regard to treatment access, the universal health coverage system may be attributable to the reduction in the SES gap for stomach cancer *mortality*. However, for prevention, the SES gap for cancer screening may exist because municipalities provide cancer screening for homemakers and workers in small companies; health insurance groups at workplaces

Table 2
Odds ratios for each socioeconomic status associated with risk for female breast and overall cancer incidence.

		Control, %	Case, %	Model 1[a]		Model 2[b]	
				OR (95% CI)	*P*	OR (95% CI)	*P*
Breast							
n		122,414	24,983				
SES							
Blue-collar industry	Blue-collar worker	12.9	12.1	1.00		1.00	
	Service worker	5.6	5.9	1.13 (1.05–1.21)	.002	1.12 (1.04–1.21)	.002
	Professional	0.3	0.3	1.09 (0.83–1.42)	.55	1.07 (0.82–1.40)	.63
	Manager	0.3	0.2	0.82 (0.56–1.20)	.30	0.83 (0.57–1.21)	.31
Service industry	Blue-collar worker	3.1	2.8	0.97 (0.88–1.07)	.53	0.98 (0.89–1.08)	.69
	Service worker	17.6	18.4	1.12 (1.06–1.20)	< .001	1.13 (1.06–1.21)	< .001
	Professional	0.4	0.5	1.58 (1.27–1.96)	< .001	1.60 (1.29–1.98)	< .001
	Manager	0.3	0.4	1.21 (0.94–1.56)	.13	1.22 (0.95–1.57)	.11
White-collar industry	Blue-collar worker	0.5	0.5	0.99 (0.81 – 1.22)	.95	1.01 (0.82–1.24)	.91
	Service worker	7.5	7.8	1.13 (1.05–1.22)	.001	1.13 (1.05 – 1.21)	.001
	Professional	7.6	7.7	1.10 (1.03–1.18)	.007	1.09 (1.02–1.17)	.01
	Manager	0.2	0.2	0.81 (0.54–1.21)	.29	0.81 (0.53–1.23)	.31
Others	Others	11.0	11.0	1.07 (0.99–1.16)	.08	1.09 (1.01–1.18)	.03
	Homemaker	32.8	32.2	1.06 (0.99–1.12)	.08	1.06 (1.00–1.13)	.05
Smoking							
	Never	68.9	73.0			1.00	
	≤20 pack-year	25.9	21.6			0.76 (0.73–0.80)	< .001
	> 20–40 pack-year	4.3	4.4			0.92 (0.85–0.98)	.02
	> 40 pack-year	0.9	1.0			0.99 (0.85–1.14)	.86
Alcohol consumption							
	Never	60.0	61.3			1.00	
	≤15 g/day	20.8	17.6			0.87 (0.83–0.91)	< .001
	> 15–30 g/day	15.9	17.3			1.12 (1.06–1.19)	< .001
	> 30 g/day	3.4	3.8			1.16 (1.06–1.26)	< .001
Overall							
n		703,157	143,806				
SES							
Blue-collar industry	Blue-collar worker	14.7	15.1	1.00		1.00	
	Service worker	4.4	4.5	1.00 (0.97–1.04)	.92	1.00 (0.96–1.04)	.97
	Professional	0.2	0.2	0.86 (0.73–1.00)	.06	0.85 (0.73–0.99)	.04
	Manager	0.3	0.3	0.87 (0.76–0.99)	.03	0.85 (0.75–0.97)	.02
Service industry	Blue-collar worker	2.7	2.6	0.96 (0.92–1.00)	.07	0.95 (0.91–1.00)	.04
	Service worker	14.4	15.2	1.04 (1.01–1.06)	.002	1.02 (1.00–1.05)	.04
	Professional	0.3	0.3	1.09 (0.98–1.21)	.11	1.09 (0.98–1.22)	.09
	Manager	0.4	0.4	0.97 (0.85–1.11)	.66	0.95 (0.83–1.09)	.48
White-collar industry	Blue-collar worker	0.4	0.5	1.01 (0.90–1.13)	.89	1.01 (0.89–1.13)	.92
	Service worker	5.7	5.5	0.95 (0.92–0.98)	.004	0.95 (0.92–0.98)	.003
	Professional	5.8	5.4	0.91 (0.88–0.94)	< .001	0.91 (0.88–0.94)	< .001
	Manager	0.2	0.2	0.84 (0.73–0.98)	.02	0.84 (0.72–0.97)	.02
Others	Others	16.5	17.1	1.00 (0.98–1.03)	.87	1.00 (0.98–1.03)	.70
	Homemaker	33.9	32.7	0.94 (0.92–0.96)	< .001	0.95 (0.93–0.96)	< .001
Smoking							
	Never	71.6	71.5			1.00	
	≤20 pack-year	24.1	22.6			0.94 (0.93–0.96)	< .001
	> 20–40 pack-year	3.4	4.5			1.28 (1.24–1.32)	< .001
	> 40 pack-year	0.9	1.4			1.58 (1.50–1.66)	< .001
Alcohol consumption							
	Never	66.0	66.9			1.00	
	≤15 g/day	19.1	16.9			0.88 (0.86–0.90)	< .001
	> 15–30 g/day	12.6	13.2			1.03 (1.00–1.06)	.08
	> 30 g/day	2.3	3.0			1.16 (1.10–1.22)	< .001

‡Data were estimated with five imputed datasets. Percentages may not total 100 because of rounding with multiple imputation. OR, odds ratio; CI, confidence interval; SES, socioeconomic status.

[a] Conditional logistic regression matched for age, admission date, and admitting hospital.

[b] Additional adjustment for smoking and alcohol consumption.

provide screening for workers in large industries (Ikeda et al., 2011; Tanaka et al., 2017). The proportion of individuals undergoing cancer screening is greater in the latter category; people with higher SES tend to undergo regular cancer screening (Chor et al., 2014; Ikeda et al., 2011; Kweon, Kim, Kang, Shin, & Choi, 2017). Indeed, in the present study, the odds for homemakers (adjusted OR 0.80) were weaker than subjects with higher SES (adjusted OR 0.67 for managers in blue-collar industries).

4.3. Lung cancer

Lung cancer is strongly socially patterned; one Swedish study found the population-attributable fraction of socioeconomic differences to be over 50% (Hemminki, Zhang, & Czene, 2003). In Japan, we still identified a steep residual inverse socioeconomic gradient even after controlling for smoking; that corresponds to a population-attributable fraction of 59% for the maximum SES gap.

Veglia et al., (2007) reported work-related secondhand tobacco smoke exposure (hazard ratio, 1.6). In particular, the blue-collar sector

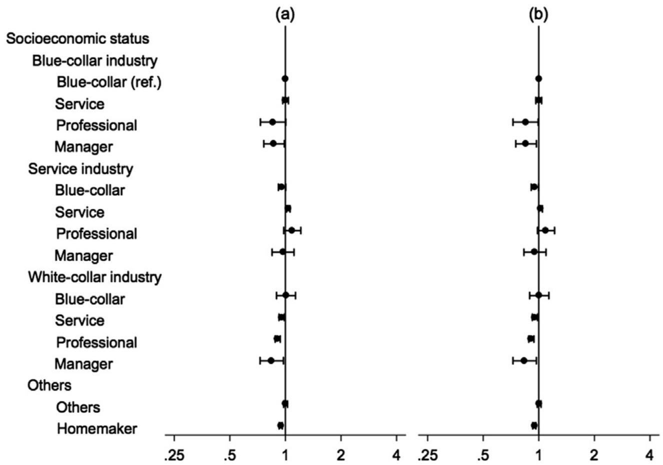


Fig. 3. Socioeconomic gradient associated with risk for overall female cancer incidence. The odds ratio (dot) and 95% confidence interval (bar) were estimated by conditional logistic regression, (a) matched for age, admission date, and admitting hospital and (b) additionally adjusted for smoking and alcohol consumption, with five imputed datasets. The numbers of cases and controls used for analysis were, respectively, 143,806 and 703,157.

workplace (e.g., manufacturing), which was the most popular workplace for women in Japan in the study period (Tanaka et al., 2017), may be more lax with regard to limiting secondhand tobacco smoke exposure (Howard, 2004). Indeed, national legislation to restrict indoor smoking has yet to be established in Japan.

4.4. Breast cancer

A positive socioeconomic gradient in breast cancer, which has been documented in many countries (Faggiano et al., 1997), may partially represent causal pathways linked to reproductive and fertility behaviors. In particular, evidence suggests that a greater risk of breast cancer incidence with higher SES is associated with relevant breast cancer risks, i.e., older age at birth of first child, use of hormone replacement therapy, and higher consumption of alcohol (Larsen et al., 2011). Indeed, alcohol consumption was associated with breast cancer risk in our study: a 12%–16% increase was evident among moderate to heavy drinkers (> 15 g ethanol per day).

We identified a positive socioeconomic gradient even after controlling for possible confounding and mediating factors. There could be potential mediation related to stress; women with higher SES are associated with interpersonal stress in the workplace (Pudrovska, Carr, McFarland, & Collins, 2013). The odds for homemakers were weaker than service workers or subjects with higher SES. This finding suggests that homemakers may have limited access to resources to promote their health (e.g., breast cancer screening) (Zaitsu et al., 2018); alternatively, homemakers may have working stress to a lesser extent at home, their main workplace. Additionally, the likelihood of undergoing breast cancer screening may be higher in individuals with higher SES, which is associated with overdiagnosis (Chor et al., 2014; Kweon et al., 2017; Jacklyn, Glasziou, Macaskill, & Barratt, 2016). With potential mediation through sleep disturbance and telomere shortening, breast cancer risk may be associated with night shift workers, such as nurses (Samulin Erdem et al., 2017; Yuan et al., 2018). In fact, we observed elevated odds among professionals in white-collar industries, which was comprised with ~40% of medical professionals, including nurses and physicians.

4.5. Remaining common cancers and less common cancers

We did not observe a socioeconomic gradient for the remaining common cancers and less common cancers. However, a possible inverse socioeconomic gradient was evident for several upper digestive and gynecologic sites, which concurs with Western trends (Faggiano et al., 1997; Spadea et al., 2010). A null socioeconomic gradient for colorectal cancer and a tendency for an inverse socioeconomic gradient for pancreatic and gallbladder cancers (which has not been consistently reported in Western countries) may be associated with healthier dietary patterns in Japan (e.g., eating more vegetables and fish) (Faggiano et al., 1997; Qiu et al., 2005; Song et al., 2016). For malignant lymphoma, a positive socioeconomic gradient has been found with some types of malignant lymphoma in the United States (Clarke, Glaser, Gomez, & Stroup, 2011). That gradient has shown mostly no association with SES worldwide (Faggiano et al., 1997), and we observed a possible inverse pattern. For other less common cancers, the literature is sparse (Faggiano et al., 1997).

4.6. Strengths and limitations

Using a large, nationwide clinical and occupational dataset, we have for the first time provided a comprehensive picture of socioeconomic inequalities in female cancer incidence in Japan. This study is one of the largest studies conducted for female cancer incidence in that country. In addition, the strengths of this study include accurate cancer diagnoses directly extracted from medical charts in contrast to less accurate ones used in previous studies with claims data (Sato et al., 2015). A further strength of the study is the relatively low job turnover in Japan, which meant less possibility of misclassification. It is estimated that on average 30% of women do not change jobs during working ages, while an additional 20% changed jobs just once (Ministry of Health, Labour and Welfare, 2014). The average length of the longest held jobs was 27 years. In contrast to previous studies, which assigned the most recent occupation as a proxy for SES recorded on the death certificate (Eguchi et al., 2017; Tanaka et al., 2017), the longest-held occupation is less likely to reflect misclassification owing to reverse causality: patients may change their jobs or become inactive in the labor force following cancer diagnosis. Although the national standard classification was revised over time, JOHAS updated the job codes to be consistent with standard practice, and we do not feel that significant misclassification was introduced (Zaitsu et al., 2016).

Some limitations, however, should be noted. First, the selection of hospital controls was subject to selection bias. The absence of relevant population-based data did not allow us to obtain population-based controls (e.g., as in a population-based case-control study in the Nordic Occupational Cancer Study) (Talibov et al., 2018); however, the analysis with the alternative control group (patients with all benign diseases) showed the same patterns and directions of the socioeconomic gradient. In addition, one-third of the missing information may have introduced selection bias—even though multiple imputation was performed; however, the sensitivity analysis with completed data showed the same socioeconomic gradient. The self-reported information on admission is another possible limitation inherent in recall bias.

Second, our measured occupational class is not a perfect proxy for SES, and other relevant socioeconomic factors, i.e., educational attainment and income levels, and the timing of the longest-held job were not assessed owing to the limitations of our dataset (Larsen et al., 2011; Spadea et al., 2010). However, a study with data from all residents in Finland showed occupational class differences in cancer incidence—even within strata of educational attainment and income levels (Weiderpass & Pukkala, 2006). In addition, our broad category of the longest-held occupational class was not designed to capture occupational exposure; therefore, it is different from detailed occupational classes defined in studies for detecting specific occupational cancer incidence (Barry et al., 2017; Talibov et al., 2018; Weiderpass & Pukkala, 2006). We could not assess the partners' SES of married women, which may be independently associated with women's SES (over and above her own occupation) (Honjo et al., 2012). Additionally, although the prevalence of each specific cancer is consistent with national statistics (Hori et al., 2015), our analyzed cases represented only 1.9% of the total cases of female cancer incidence in the whole country. Hence, the generalizability of our findings to the rest of Japan may be limited.

Finally, we assessed the contribution of major modifiable behavioral factors of smoking and alcohol consumption on the socioeconomic gradient; however, the data limitations did not enable us to assess other possible mediation factors such as diet, physical activity, and night shift work (Qiu et al., 2005; Samulin Erdem et al., 2017; Talibov et al., 2018; Takao, Kawakami, & Ohtsu, 2003; Yuan et al., 2018), or evaluate socioeconomic inequalities, including employment status (full-time, precarious, and unemployed workers) that might have potential impacts on cancer risk through psychological distress or access to healthcare service (Singer et al., 2016; Tsurugano, Inoue, & Yano, 2012), within the strata of cancer stage at diagnosis by linkage of SES information to local cancer registries (Kweon et al., 2017; Zaitsu et al., 2015). Therefore, future studies, such as ones concentrating on molecular pathological epidemiology (Ogino et al., 2016), are warranted to integrate all aspects of cancer causal pathways.

5. Conclusion

We observed socioeconomic inequalities in female cancer incidence in Japan—even after controlling for smoking and alcohol consumption. The national cancer prevention strategy in Japan needs to explicitly incorporate strategies to address socioeconomic inequalities.

Ethics approval and consent to participate

Written informed consent was obtained, and the research ethics committees of The University of Tokyo, Tokyo (Protocol Number 3890-3) and Kanto Rosai Hospital, Kanagawa (Protocol Number 2014-38) approved the study.

Availability of data and material

The data that support the findings of this study are available from JOHAS, but restrictions apply to the availability of these data; they were used under the research agreement for the current study and so are not publicly available. If any person wishes to verify our data, they are most welcome to contact the corresponding author.

Conflict of interest

The authors declare no conflict of interest.

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Authors' contributions

MZ and IK originated the idea and designed the study. MZ conducted the analysis and wrote the manuscript draft. All authors interpreted the analyses and critically reviewed and edited the manuscript. All authors read and approved the final manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.ssmph.2018.06.001.

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