



Occupational Class Groups as a Risk Factor for Gastrointestinal Cancer: A Case-Control Study

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ABSTRACT

Background: Cancer has a high mortality rate in both developing and developed countries. 11%–15% of cancers are attributable to occupational risk factors.

Objective: To determine if specific occupational classes, based on the International Standard for Classification of Occupations 2008 (ISCO-08), are risk factors for gastrointestinal (GI) cancer.

Methods: In this case-control study, 834 cancer patients were interviewed by a single physician. Cases included patients with GI cancer. Age-matched controls were selected from non-GI cancer patients. Each year of working, up until 5 years before the diagnosis, was questioned and categorized by the ISCO classification.

Results: 243 GI cancer cases and 243 non-GI cancer patients (486 in total) were studied. Working in ISCO class 8 (plant and machine operators, and assemblers) was significantly associated with higher risk of GI cancer (OR 1.63, 95% CI 1.05 to 2.52). Working in ISCO class 6 (skilled agricultural, forestry and fishery workers) and 9 (elementary occupations) were also associated with higher incidence of GI cancers.

Conclusion: Working in ISCO classes of 8, 6, and 9, which are usually associated with low socio-economic status, can be considered a risk factor for GI cancers.

Keywords: Neoplasms; Occupations; Classification; Risk factors; Epidemiology; Gastrointestinal tract

Introduction

Cancer is a disease with serious health consequences for the patients and their families.¹ In 2008, 12.7 million new cases of cancers and 7.6 million cancer deaths occurred worldwide; 56% of the new cases and 63% of the mortalities happened in the developing countries.² Gastrointestinal (GI) malignancies can be divided roughly into cancers of the esoph-

agus, stomach, small intestine, colon, and rectum.³

In Iran, cancer is the third leading cause of death. GI cancer is the most significant cause of cancer-related deaths in Iranian males (up to 50%).⁴ The most prevalent sites of GI tract involved in decreasing order include the stomach, colon, rectum, and esophagus.⁴ The incidence of colorectal cancer ranks third (after the lung and breast cancer) among cancer types. The

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number of new cases reported worldwide was 1 234 000 in 2008.² Gastric cancer ranks fourth in the number of cancers reported worldwide; it is the second most common cause of death due to cancer.⁴ Esophageal cancer is also common and its incidence is high in Iran, as part of the Asian esophageal cancer belt.⁴

GI cancer has many risk factors. However, diet has the most significant effect on colorectal cancers. Low levels of physical activity, cigarette smoking, a positive family history of cancer, low socio-economic status, and the use of alcohol are common risk factors for GI cancers.⁵ The level of poverty, sex, and race have also been associated with the occurrence of colorectal cancers;⁶ 5%–15% of colon cancers are familial. Familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC) are among these hereditary colorectal cancers.⁵

Occupational and environmental risk factors for GI cancers are now in the center of attention.⁵ Every year, occupational exposures cause 40 000 cases of cancer and 20 000 cancer deaths in the USA.⁷ There is increased odds ratio for the occurrence of GI cancers in many occupations including leather industry, basic metals production, plastic and rubber manufacturing, and also workers who repair and install machinery who are exposed to asbestos. In total, exposure to chemicals has been a significant risk for colorectal cancers.⁵ The excess risk

attributable to occupational risk factors has been estimated to range from 11% to 15%.⁵ A reduction in the incidence of GI cancers in agricultural workers has also been observed; it can be attributable to lower rates of smoking and higher physical activity.⁸ Job titles and classifications have been linked to socio-economic class of workers or their families.⁹ There are studies that demonstrate higher mortality rates among skilled, semi-skilled, and unskilled workers compared to managerial and professional workers.¹⁰

The objective of this study was to determine whether specific occupational classes, based on the International Standard for Classification of Occupations 2008 (ISCO-08), are risk factors for GI cancer.

Patients and Methods

Our study population consisted of patients with confirmed diagnosis of cancer undergoing chemotherapy or surgical interventions who were hospitalized in one of the hospitals in Tehran, northern Iran. This hospital was a general hospital with all the specialty and subspecialties in medicine and a referral center for cancer patients from all over the country.

Only patients with biopsy-proven cancer were included in this case-control study. Only male patients were included for easier matching and also due to the fact that most women in Iran do not work and spend their times doing home chores. Our cases consisted of GI cancer patients. We only included patients with esophageal, gastric, small intestinal, and colorectal cancers, and excluded hepatic, biliary, and pancreatic cancers because of possible non-GI origin of the malignancy in these organs; these cancers may also have different risk factors that could confound our study. The controls were selected from other (non-GI) cancer patients. Each of controls was matched with a case based

TAKE-HOME MESSAGE

- 11%–15% of cancers are attributable to occupational risk factors.
- Working as plant and machine operators, and assemblers (ISCO class 8), Skilled agricultural, forestry and fishery workers (ISCO class 6), and elementary occupations (ISCO class 9) (lower socio-economic status) can be considered a risk factor for the occurrence of gastrointestinal cancers.

on his age at the time of diagnosis. Only patients aged between 40 and 70 years at the time of diagnosis, were included in the study. We chose controls from other cancer patients because this hospital was a referral center for cancers from all over the country so that the source population of cases and controls would be the same. This would have not been true for benign disorders. Cancer patients who were hospitalized for both chemotherapy and surgical interventions were included. The interviewed patients were not necessarily new cases. Because many brain tumor patients could not be interviewed and due to the possible effects of amnesia (causing recall bias), we excluded them from the controls. All of the cases and controls were interviewed by a single physician to reduce inter-personal variations. The interviewer was not blinded to the diagnosis of study participants. The duration of the study was 15 months—from June 2014 to September 2015. Exclusion criteria were positive history of cancer in the family (not necessarily the same type of cancer the patient had), work experience less than five years, and no occupational history beyond five years before the diagnosis of cancer.

The Interview

The interview was performed during the patients' stay in hospital by one physician to reduce inter-personal differences. Those patients who did not give informed consent after the purpose of the study was explained to them, were not interviewed. The role of the companions of the patients was only auxiliary and data were only entered with the patient's approval. The interview consisted of a comprehensive assessment of the occupational (vocational) history, simple lifestyle indicator questionnaire (SLIQ) for assessment of the lifestyle and some other questions (*eg*, marital status, level of education, and shift work). Those patients who fulfilled the inclusion criteria

were interviewed and asked about the occupational history from childhood up until five years before the diagnosis of their cancer; duration of each occupation was also asked. Even the occupations performed in childhood, part-time occupations, or seasonal occupations were asked with detail. If a patient had history of working in several occupations, each job would be written separately with its duration. The five years were considered because of the latency for development of overt cancer and the span of time from the onset of the disease and its diagnosis. Demographic data included age, marital status, cigarette smoking, history of shift work, and living in rural or urban areas for most of the life since birth. Information about family history of cancer and lifestyle was also asked.

The SLIQ questionnaire inquires about the diet (use of vegetables, fruits and whole grain), exercise (light, moderate, and vigorous physical activities), alcohol consumption, smoking, and perceived stress level.¹¹ It scores the variables from '0' to '2.' For diet, higher scores mean more frequent consumption of fruits and vegetables and for physical activity, higher scores mean more vigorous activities with higher frequency. For alcohol, smoking, and life stress, higher scores mean lesser consumption of alcohol, negative history of smoking, and lower stress, respectively; scoring high in all these variables means healthier lifestyle. Its validity and reliability has been investigated in previous studies.¹² Because every patient who was hospitalized in this hospital had to have a complete blood count (CBC), we also considered the participants' red blood cell (RBC) counts, hemoglobin levels, and platelet counts. Because of the possibility of the transfusion during the hospitalization, we noted admission CBCs, which were taken before any interventions were performed. White blood cell count was excluded due to many confounders.

Table 1: Demographic data presented either as mean (SD) or n (%)

Variable	Cases (n=243)	Controls (n=243)	p value
Shiftwork (yrs)	0.89 (3.26)	1.37 (4.20)	0.193*
Smoking (pack-yrs)	1.89 (4.32)	3.29 (6.59)	0.071*
RBC count ($\times 10^6/\mu\text{L}$)	3.79 (0.52)	3.74 (0.51)	0.265
Hemoglobin (g/dL)	12.42 (1.44)	12.24 (1.39)	0.160
Platelet count ($\times 10^3/\mu\text{L}$)	208.23 (67.68)	177.57 (86.60)	0.001
Years since diagnosis	2.60 (1.89)	2.69 (1.88)	0.545*
Body mass index (kg/m ²)	26.48 (2.99)	26.95 (3.01)	0.089
Marital status			
Married	221 (90.9%)	219 (90.1%)	0.877
Single or divorced	22 (9.1%)	24 (9.9%)	
Residence			
Urban	151 (62.1%)	165 (67.9%)	0.216
Rural	92 (37.9%)	78 (32.1%)	
Smoking history			
Positive	46 (18.9%)	59 (24.3%)	0.186
Negative	197 (81.1%)	184 (75.7%)	
Shiftwork			
Positive	25 (10.3%)	34 (14.0%)	0.266
Negative	218 (89.7%)	209 (86.0%)	
Level of education (yrs)			
0	16 (6.6%)	18 (7.4%)	0.787
1–6	62 (25.6%)	58 (23.9%)	
7–12	94 (38.6%)	87 (35.8%)	
>12	71 (29.2%)	80 (32.9%)	
Stress level score			
0	25 (10.3%)	22 (9.0%)	0.889
1	99 (40.7%)	102 (42.0%)	
2	119 (49.0%)	119 (49.0%)	
Activity level			
Light	25 (10.3%)	25 (10.3%)	0.929
Moderate	99 (40.7%)	103 (42.4%)	
Vigorous	119 (49.0%)	115 (47.3%)	
Diet score			
0	59 (24.3%)	64 (26.3%)	0.857
1	132 (54.3%)	130 (53.5%)	
2	52 (21.4%)	49 (20.2%)	

*Calculated using non-parametric tests due to skewed distribution

The occupations asked during the interview were categorized into 10 different job classes based on the ISCO-o8.¹³ This classification or its older versions were used in many studies on cancer.^{14,15} In this classification, job activities are grouped in terms of specific tasks and duties for that job. Skill specialization and skill level are the two dimensions that this classification is based on. The former is a criterion of competence and professionalism and the latter is about the complexity of the job. Different ISCO groups have different job characteristics.¹⁶ The major groups consist of: 1) Managers; 2) Professionals; 3) Technicians and associate professionals; 4) Clerical support workers; 5) Service and sales workers; 6) Skilled agricultural, forestry and fishery workers; 7) Craft and related trades workers; 8) Plant and machine operators, and assemblers; 9) Elementary occupations; and 0) Armed forces.¹³ The number of working years in any category was noted. The person who performed the coding was blinded to the type of cancer. Only the one-digit major occupational groups were chosen so we could have enough power. If a person had worked in more than one occupational category, the number of years in each category was noted accordingly. The number of years was averaged for each category for cases and controls. The mean years of working in each category was compared between the cases and the controls.

Each GI cancer case was age-matched with a patient with another type of cancer. There was no need for matching for the interviewer (only one interviewer was involved in the whole study), the hospital of admission, and sex due to the study design.

Ethics

This study was approved by the Ethics Committee of Iran University of Medical Sciences, Tehran, Iran. Informed consent

was acquired before inclusion of patients in the study. All the interviewed patients knew the purpose of the study and agreed to share their lab data. If a patient refused to cooperate during the interview, he was excluded from the study without any consequences for him.

Statistical Analysis

The occupational classes (as exposures) were averaged between the two groups. *Student's t* test was used to define the difference in the means between the GI cancer group (cases) and other cancers group (controls). χ^2 test was used for comparing categorical variables. Working in an occupational class was categorized as “ever-workers” (those who have worked in that class) and “never-workers” (those who had never worked in that class). The ever-workers were further divided into those with fewer than 15 years of experience and those with 15 or more years of experience. Binary logistic regression analysis was used to determine the odds ratios pertinent to each occupational class. A two-tailed *p* value <0.05 was considered statistically significant.

Results

From 988 patients who fulfilled the inclusion criteria, 834 cancer patients agreed to be interviewed (response rate of 84.4%). The number of patients with GI cancer and patients with non-GI cancer were 322 and 512, respectively. Fifty-five of the GI cancer patients had positive family history of cancer in their first-degree relatives and thus, were excluded from the study. Only seven patients were grouped into the ISCO classes of 1 and 0, and we decided to exclude them from the study too (even those who had worked for a limited amount of time in these classes were excluded). Four patients referred from other countries (Iraq and Afghanistan), were also excluded.

Ten patients with jobs not classifiable by ISCO classification (mostly illegal activities), were also excluded. For three cases we could not find suitable age-matched controls; they were also excluded. At last 243 patients with GI cancer were included in our study. The above mentioned exclusion criteria were applied to the controls; then, 387 non-GI cancer patients remained. From these patients, 243 age-matched controls were selected.

Table 1 shows the demographic data of these 486 patients. The mean age of both groups at the time of diagnosis was 50.9 (SD 6.0) years. The mean age of the cases was 53.5 (SD 6.1) and of the controls was 53.6 (SD 6.0) years.

The types of GI cancers in our cases were gastric cancer (36.6%), cancer of colon (31.7%), cancer of rectum (18.5%), esophageal cancer (8.6%), and small intestinal cancer (4.5%). The types of cancers in the controls were hematologic cancers (33.3%); urinary and reproductive tract cancers (32.1%); thyroid cancers (16.9%); pulmonary, pleural, and upper airway cancers (13.2%); and other types of cancer (4.5%).

Table 2 presents the comparison between the mean years of working in different occupational classes between cases and controls. Only the mean years of working as plant and machine operators (ISCO group 8) was significantly (*p*=0.049) different between the cases and controls. The mean years working in the ISCO group 8 in cases was almost 1.5 years higher than that in the controls (Table 2). For each year of extra-work in this class, the risk of developing GI cancer increased by 2%.

We assessed the odds ratios of ever-working in an ISCO group *vs* never-working in that group (Table 3). All patients that had ever worked in an ISCO group were compared with those who had never worked in that group for the frequency of GI *vs* non-GI cancers. Here, again only the

Table 2: Quantitative assessment of work history in different ISCO groups

Occupational class (ISCO group)	Mean years of work history in each class		95% CI for the difference between means	OR (95% CI)*
	Cases (n=243)	Controls (n=243)		
Professionals (2)	0.329	0.230	-0.524 to 0.326	1.02 (0.94 to 1.1)
Technicians (3)	0.794	1.102	-0.490 to 1.107	0.99 (0.95 to 1.03)
Clerks (4)	2.707	2.567	-1.414 to 1.134	1.00 (0.98 to 1.03)
Service and sales (5)	1.971	2.415	-0.701 to 1.590	0.99 (0.96 to 1.02)
Skilled agricultural, forestry and fishery (6)	4.094	4.214	-1.424 to 1.663	1.0 (0.98 to 1.02)
Craft (7)	4.193	4.679	-1.133 to 2.104	0.99 (0.98 to 1.01)
Plant and machine operators (8)	5.053	3.567	-2.966 to -0.004	1.02 (1.00 to 1.04)
Elementary occupations (9)	3.238	3.876	-0.797 to 2.073	0.99 (0.97 to 1.01)

*Calculated using binary logistic regression (dependent variable: having GI cancer, independent variable: years of working in corresponding ISCO classifications)

ISCO group 8 was with an odds ratio of 1.63 (95% CI 1.05 to 2.52) was an independent risk factor. No significant difference was found between the most prevalent job and occupational class of the patients (Table 4).

The patients were categorized into three groups based on their history of work in any ISCO groups: 1) those who never worked in that group, 2) those who had worked <15 years in that particular group, and 3) those who had worked 15 years or more in that group. Odds ratios for those groups who had worked in the particular ISCO group were calculated and then compared with those who had never worked in that group. Working <15 years in ISCO groups 6 and 9 were significant (Table 5).

Discussion

This study showed that working as plant and machine operators (ISCO class 8), skilled agricultural, forestry and fishery (ISCO class 6), and elementary occupations (ISCO class 9) was associated with higher risks for GI cancers. This associa-

tion was more pronounced for the ISCO class 8 with an odds ratio of 1.02 (95% CI 1.00 to 1.04) for each year of extra-work in this class, and an odds ratio of 1.63 (95% CI of 1.05 to 2.52) for ever-working in this class in lifetime. The ISCO classes 6 and 9 were in the second level of significance.

In a somewhat similar study on 1155 patients with colon cancer in British Columbia, the independent risk factors were working in fabricating, assembling and repair of wood products (ISCO class 7), insurance sales jobs (ISCO class 3), mechanics and repairers of rail jobs (ISCO class 8), brick and stone mason-tile settlers (ISCO class 7), and ship engineering officers (ISCO class 3).¹⁷ There were however, many differences in methodology between our study and that study. The British Columbia study was a questionnaire-based study that divided the occupations into 1104 industry titles and 597 occupational titles, which significantly reduced the power of the study. We chose to perform our study in a stepwise manner. We tried to find the one-digit occupational classes with the most significant risk and then

Table 3: Odd's ratios and significance level of the ever-worked category

Occupational class (ISCO group)	Number of cases	Number of controls	Unadjusted OR* (95% CI)
Professionals (2)	4	3	1.34 (0.30 to 6.05)
Technicians (3)	10	12	0.83 (0.35 to 1.95)
Clerks (4)	31	29	1.08 (0.63 to 1.85)
Service and sales (5)	27	29	0.92 (0.53 to 1.61)
Skilled agricultural, forestry and fishery (6)	51	47	1.11 (0.71 to 1.73)
Craft (7)	51	52	0.98 (0.63 to 1.51)
Plant and machine operators (8)	63	43	1.63 (1.05 to 2.52)
Elementary occupations (9)	46	46	1.00 (0.64 to 1.57)

*Calculated using crosstabs

will continue the study on high risk groups within two-digit occupational classes and so on.

In another case-control study in India on 703 patients, long-term exposure to animals (that can be associated with lower socio-economic occupational class) was shown to be associated with esophageal cancer.¹⁸ A systematic review showed that lower socio-economic jobs are associated with higher incidence of gastric cancer, however, it is not true for the level of

income.¹⁹ In a case-control study in Taiwan on 326 patients, it was shown that exposure to dust and also gardening and farming (ISCO classes of 6 and 9) are associated with the occurrence of esophageal cancer.²⁰ A case-control study in Spain on 399 gastric cancer patients, revealed that having occupations like cooks (ISCO class 5), wood processing plant operators (ISCO class 8), and food and related product machine operators (ISCO class 8) are associated with higher incidence of gas-

Table 4: Classification of cases and controls based on their most prevalent occupational class in life

Occupational class (ISCO group)	Number of cases	Number of controls	OR* (95% CI)
Professionals (2)	3	3	1.00 (0.20 to 5.00)
Technicians (3)	10	12	0.83 (0.35 to 1.95)
Clerks (4)	31	29	1.08 (0.62 to 1.85)
Service and sales (5)	26	25	1.05 (0.58 to 1.86)
Skilled agricultural, forestry and fishery (6)	43	46	0.92 (0.58 to 1.45)
Craft (7)	46	46	1.00 (0.63 to 1.57)
Plant and machine operators (8)	55	42	1.40 (0.89 to 2.19)
Elementary occupations (9)	29	40	0.69 (0.41 to 1.15)

*Calculated using binary logistic regression (dependent variable: having GI cancer, Independent variable: most prevalent occupation based on ISCO classification)

Table 5: Odd's ratios and significance level of the work class with a cut-point of 15 years

Occupational class (ISCO group)	Working history*	Number of cases	Number of controls	OR (95% CI)
Professionals (2)	<15 yrs	1	1	1.00 (0.06 to 16.15)
	≥15 yrs	3	2	1.51 (0.25 to 9.10)
Technicians (3)	<15 yrs	2	1	1.98 (0.18 to 22.02)
	≥15 yrs	8	11	0.72 (0.29 to 1.83)
Clerks (4)	<15 yrs	2	1	2.02 (0.18 to 22.4)
	≥15 yrs	29	28	1.05 (0.60 to 1.82)
Service and sales (5)	<15 yrs	6	7	0.85 (0.28 to 2.57)
	≥15 yrs	22	21	0.95 (0.51 to 1.77)
Skilled agricultural, forestry and fishery (6)	<15 yrs	8	1	8.17 (1.01 to 65.92)
	≥15 yrs	43	46	0.95 (0.60 to 1.51)
Craft (7)	<15 yrs	9	9	1.00 (0.39 to 2.56)
	≥15 yrs	42	43	0.97 (0.61 to 1.56)
Plant and machine operators (8)	<15 yrs	7	2	3.89 (0.80 to 18.96)
	≥15 yrs	56	41	1.52 (0.97 to 2.38)
Elementary occupations (9)	<15 yrs	18	6	3.00 (1.17 to 7.72)
	≥15 yrs	28	40	0.70 (0.42 to 1.18)

*Compared with no working history in that particular group
 **Calculated using binomial logistic regression

tric cancers.²¹ In a study in Europe on 101 patients with small intestine carcinoid tumor, it was found that manufacture of the bodies of motor vehicles (ISCO class 8), footwear (ISCO class 8), and metal structures (ISCO class 8) are at higher risk of this neoplasm.²² There are also studies that show working under heat stress (usually in lower socio-economic workers), is associated with gastric cancer.²³ In many of the above-mentioned studies, it is hard to define the exact ISCO occupational class because of the widespread use of many coding systems. It is prudent to use a standard system for occupational classifications for future meta-analyses.

We found no significant difference between cases and controls in terms of the

lifestyle and other demographic risk factors. The only significant difference was a lower platelet count in controls, which can be due to the presence of patients with leukemia/lymphoma, which usually have lower platelet count.²⁴ Low vegetable and fruit intake is considered a risk factor for colorectal cancers.²⁵ In our study there was however, no difference between their consumption between the cases and controls.

We chose the cut-point of 15 years for dividing our cases and controls in some analyses because in some previous studies it was used for this purpose; it has also been considered a critical cut-point in other GI cancers.²⁶ There were only a few number of patients in the ISCO classes 1 and 0. We therefore decided to exclude

them from the study. Furthermore, patients working in ISCO class 1 (the managers) have usually a higher socio-economic level and probably prefer private hospitals. Patients in ISCO class 0 (the armed forces) in Iran, have specific insurance system and attend particular hospitals and usually do not attend the general public hospitals.

Our study had some limitations. This study was only performed on men. We did not directly assess the exposure levels and only the occupational title was used. The number of hours working in a day and the level of exposure to other probable carcinogens were not assessed. We know that many carcinogens are environmental and are not related to the occupation of the person. There may be synergistic effects between occupational and non-occupational factors. Nevertheless, we tried to reduce the influence of these variables by matching the cases and controls. We only studied occupations, not exposure, thus, we cannot discuss the association between GI cancer and specific exposures like diesel exhaust, asbestos, *etc*. Because the data pertinent to occupational classes are easily available, using these classes can be important when no exposure data are available. In this study, there was no difference between the diets, physical activities, and level of perceived stress among cases and controls. Because alcohol consumption is punishable by law in Iran, people usually deny its use. We therefore excluded this variable from our study (only eight persons mentioned its consumption). The same was true for the use of illicit drugs (narcotics, cannabis, *etc*); they were also excluded from the study. Occupational subcategories were not included in our study because dividing the categories would have caused reduced power, as it was the case in previous studies with even larger number of cases and controls.^{17,27} Recall bias is an inseparable part of case-control studies. By using patients with non-GI cancers as controls, we

tried to reduce the differences in recall bias that would have happened with non-cancer controls. We did not directly assessed the socioeconomic levels of patients; some of the associations can be attributable to this variable, but we hope our classification was took into account this variable to some extent; assessing this variable would have resulted in overmatching. Sometimes when socio-economic data are not available, occupational classes can be used as surrogates. This article did not provide a dose-response relationship between the exposure and outcome variables. Future studies with higher number of cases might be able to overcome this shortcoming.

Using cancer patients as controls (as opposed to hospital controls) was a one of the strengths in our study because it reduced interview bias and recall bias. Moreover, the source populations were similar because both are referred from all over the country to the same hospital. Our data gathering was conducted by direct interview with the patients. Using one interviewer and asking the same questions in similar environments and almost the same duration for the interview, helped reduce many possible biases (*eg*, inherent biases pertinent to the use of questionnaires, *etc*). The process of data gathering and analyses was performed by a team of physicians specialized in occupational medicine. Racial differences were not of concern in our study because there was only one dominant race in Iran (all Caucasian); none of the patients were from different races. The case-control design of the study was most appropriate for evaluating relatively rare diseases like cancer and it is commonly used in the field of occupational medicine. Occupational classes are a mixture of different exposures. No one in any particular occupations is solely exposed to a single carcinogen. There are great correlations between exposures.²⁸ Using occupational class as a risk factor helps us to include all

of these exposures as a single risk factor. Using ISCO classification, which divides the occupations into 10 major categories and then divides them into minor subcategories, helps us in future research and assessment of more specific occupations included in high-risk major categories. This also means that many exposures are grouped in the same category, which might not be similar, but future studies may be able to define the exact exposures responsible for higher number of cancers in a particular group. Using quantitative measure of occupations (years of work) and comparing them between cases and controls reduces the effects of a possible bias of not differentiating between one year of work or 30 years of work history in an occupational class.

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