Epidemiological Risk Factors for Cancers of the Lung, Breast, Colon-rectum & Oral cavity: A case-control study in the Philippines

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ABSTRACT

Introduction. In the Philippines, lung, breast, colon-rectum, and oral cavity cancers are among the top 10 most common cancers. This study evaluates the risk factors for these cancers among Filipinos.

Methods. This age-matched case-control study included incident primary cancers (histologically-diagnosed) of the lung, breast (also matched for sex), colon-rectum and oral cavity. Controls (clinically free and no history of cancer) were obtained from the same tertiary hospitals as the cases. Target sample size was 283 cases and 283 controls per cancer type. Conditional logistic regression was done.

Results. Exposure to cigarette/tobacco was a significant risk factor for lung (OR of current smoker compared to non-smoker [95% Confidence Interval]: 3.6 [1.6-7.9]) and oral cavity cancers (2.0 [1.2-3.3]); family history (1st degree) for lung (4.3 [1.3 – 14.2]) and breast cancers (3.0 [1.2-7.5]); every year increase in age at first pregnancy for breast cancer (1.06 [1.02-1.11]). Other risk factors for oral cavity were passive smoking (2.8 [1.6-5.1]), chewing tobacco (5.2[1.4-19.5]) and inverted cigarette smoking (3.2[1.3-8.1]). Fish sauce (patis) was found to be a protective factor for breast cancer (0.34 [0.22-0.51]) and oral cavity (0.44 [0.25-0.78]) and use of shrimp paste (bagoong) (0.48 [0.27-0.84]) for oral cavity.

Conclusion and Recommendations. Except for family history of cancer, the identified risk factors for lung, colon-rectum, and oral cavity cancers are preventable. Proper diet and lifestyle, avoidance of cigarettes and tobacco, and environmental safety in the workplace are key cancer prevention measures. Public awareness campaign and continuing healthcare provider education must always be part of a cancer prevention program.

Keywords: lung neoplasm, breast neoplasm, colon neoplasm, oral cavity neoplasm, cancer risk factor, Philippines

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Introduction

Non-communicable diseases create an ever-growing proportion of the burden of ill health in developing countries. Cancer has always had a significant impact and its relative importance has grown with the increasing emphasis on the economic and social consequences of ill health and premature death in the adult age range. In the Philippines, cancers of the lung, breast, colon-rectum, and oral cavity have always ranked within the top 10 most common cancers.

Lung cancer is the most common tumour in the world.[1] In the Philippines, lung cancer ranks first with age-standardized incidence and mortality rates for the world population (ASR-W) of 50.2 and 46.4 per 100,000 males and 13.2 and 12.6 per 100,000 females.[2]

Identified risk factors for lung cancer are tobacco smoking, environmental tobacco smoke, air pollution, indoor radon, occupational respiratory carcinogens (arsenic, asbestos, bis-chloromethyl ether, chromium, nickel, polycyclic aromatic compounds, vinyl chloride), high fat diet, and previous non-neoplastic lung diseases (tuberculosis, pulmonary fibrosis or silicosis, chronic bronchitis, emphysema).[3]

Breast cancer is the third most common cancer in the world,[1] despite the fact that it is confined almost entirely to the female sex. Breast cancer incidence rates are rising in several developing countries and it is already the most frequently occurring female cancer in many countries. In the Philippines, breast cancer ranks second most common cancer among both sexes, and first among women, with incidence rates being the highest recorded in any Asian population (with the exception of the Jewish population of Israel). The incidence appears to be similar to that observed in Southern and Central Europe.[2] Reasons for such elevated incidence were not clear. In 1994, Ngelangel et al.[4] did a case-control study concluding that similar risk factors were found as in other studies, particularly among Chinese in Taiwan.[4]

Colon-rectal cancer ranks 2nd in terms of incidence and mortality in more developed countries in the world.[1] In the Philippines, colon-rectal cancer ranks within the top 10 cancers with incidence (and mortality) of 18.8 (12.1) per 100,000 ASR-W among males and 14.8 (9.5) per 100,000 ASR-W among females.[2]

Identified risk factors for colon-rectal cancer are familial adenomatous polyposis, chronic ulcerative colitis, familial cancer syndromes, adenomatous polyps, and high-meat or fat diet and low fiber intake.[1]

Oral cavity cancer has an ASR-W of 6.3 per 100,000 population among males and 3.2 per 100,000 among females.[1] In the Philippines, oral cavity cancer ranks 11th most common cancer in Filipino males with 5.7 per 100.000 ASR-W and in females with 4.7 per 100,000 ASR-W.[2]

The oral cavity extends from the skin-vermillion junctions of the anterior lips to the junction of the hard and soft palates above and to the line of circumvallate papillae below and includes the lips, the anterior two-thirds of the tongue, the buccal mucosa, the floor of the mouth, the lower gingiva, the retromolar trigone, the upper gingiva, and the hard palate.

It is predominantly ectodermal in origin, and 90% of cancers from this site are squamous cell carcinomas.[3]

Identified risk factors for oral cavity cancer are cigarette smoking, pipe smoking, tobacco chewing, reverse cigarette smoking, heavy alcohol intake, betel quid chewing, poor oral hygiene and chronic trauma from broken teeth or ill-fitting dentures.[3]

This study evaluates the risk factors for cancers of the lung, breast, colon-rectum and oral cavity among Filipino patients. For breast cancer, this study also evaluates several factors not previously studied in the Philippines, such as diet and exposure to environmental chemicals.

Methods

This case-control study was conducted from June 2002 to September 2008. Cases (any age, any stage, any ECOG [Eastern Clinical Oncology Group performance status]) included incident histologically diagnosed primary cancers of the lung, breast, colon-rectum and oral cavity from seven tertiary hospitals (Philippine General Hospital [PGH], Jose R. Reyes Memorial Medical Center [JRRMMC], Ospital ng Maynila Medical Center [OMMC], Corazon Locsin Montelibano Memorial Regional Hospital [CLMMRH], Medical Center Manila [MCM], East Avenue Medical Center [EAMC], and Lung Center of the Philippines [LCP]). Cases were those with histologically or cytologically proven cancer with no history of chemotherapy or radiotherapy prior to enrolment to this study. Sample tissues (tissue biopsy or aspiration, pleural washings or fluid, oral washings or swab) were obtained from each subject. Classification was further verified by obtaining the histopathology result of the patient's tissue. In the event of a study participant being initially classified as a case but whose histopathology result showed non-cancer diagnosis, final classification was made by the coordinating physician and the pathologist of the hospital where the patient was recruited.

Age-matched controls (five-year interval) were randomly selected from the outpatient clinics of the same hospitals as the cases. For breast cancer, controls were also matched by sex. Controls had no history of cancer and were clinically free of cancer by physical examination, endoscopy or bronchoscopy and radiology (imaging, x-ray, ultrasound, CT scan and mammography).

Health worker-interviewers, who were unaware of the objectives and hypotheses of the study, were trained to interview both cases and controls in a standardized manner. The questionnaire was patterned on several similar cancer and diet or environmental exposure questionnaires mostly done in the United States. The questionnaire together with the interview techniques (which were likewise standardized) were pre-tested on a group of Filipino patients. Necessary modifications were done. The interviews were conducted in the hospital or clinic where the study participants (who were not told the specific risk factors being studied for particular cancer types) were recruited. Unblinding of interviewers as to case-control status was not avoided as the study progressed.

Ethical committee approval was obtained from the University of the Philippines College of Medicine Research Implementation and Development Organization, with a technical review by the Philippine Council for Health & Research Development. Informed consent for participation of each patient recruited into the study was obtained prior to any study-related procedure such as the interview and acquisition of histopathological specimens from the cases. All data collected from the study participants were treated as confidential.

Data from the interviews were supplemented by medical chart review. Information collected were 1) demographic variables (age, sex); 2) medical history (cancer); 3) family history of cancer (first degree); 4) smoking experience including tobacco chewing, inverted cigarette smoking and smoking status (whether current, ex-smoker, or no-smoker); 5) betel quid chewing 6) alcohol consumption; 7) oral contraceptive use; 8) consumption of preserved or canned food; 9) *patis* (salty fish sauce) or *bagoong* (shrimp paste) consumption; 10) vegetable consumption; 11) consumption of food preserved by nitrates or nitrite; 11) consumption of cured, smoke-preserved, salted-preserved food; 12) consumption of scalding hot food; and 13) exposure to chemicals or other risk factors in the environment for more than a year. Environmental risk factors considered were exposure to a) moldy food; b) pesticide; c) vinyl chloride factories; d) benzene-containing factories such as rubber, tire-curing or building and leather factories; e) UV radiation; f) coal carbonization factories such as coal gas, tar, pitch; and g) wood dust-furniture factories. For breast cancer: 1) medical history of fibrocystic breast disease; 2) obesity; 3) age at menarche; 4) age at first pregnancy; 5) menopause; 6) number of pregnancies; and 7) oral hormonal pill contraceptives or hormone replacement therapy (HRT).

Sample Size

In order to detect an odds ratio (OR) of at least 1.75 at α=0.05 (2-sided test), β=0.20 (with exposure rate of the factor of smallest cancer risk in the general population to be 19%), while matching one case to one control, the minimum target number of cases needed for each cancer type is 283. A minimum total of 566 case-control pairs are needed.

Data Analysis

Separately for cases and controls and for each cancer type, the mean and standard deviation of age in years and the frequency and percentage of male patients were generated. For each cancer type, considering the matching by age (and for breast cancer, also matching by sex) as well as the unequal matching (some cases have more than one control), crude odds ratio was estimated at 95% confidence level for each suspected risk factor. After this bivariate analysis, multivariate analysis was done as follows: 1) Factors with p-values < 0.20 based on the bivariate analysis were identified as the initial set of candidate predictors; 2) these predictors were included in the conditional logistic regression analysis to generate adjusted ORs and corresponding p-values; 3) the final model was generated considering only risk factors with ORs that are significant at α=0.05 (2-tailed). The predictors in this model were identified as the predictors for the particular cancer type.

Results

A total of 816 cancer cases (lung=119, colon-rectal=224, oral cavity=176 and breast-297) and 1120 controls were included. Note that 119 oral cavity control females also served as the controls of the breast cancer cases. Note further that 90 controls for breast cancer consented to blind fine needle aspiration biopsy (FNAB). All were negative.

Due to slow recruitment of cases, achievement of 283 cases per cancer type had been difficult. To address the expected decrease in power, the research team then decided to recruit more controls. Table 1shows the age and sex distribution of cases and controls.

Different sets of factors associated with each cancer type were identified.

1. **Lung** – By bivariate analysis (age-matched), cigarette

smoking (current, ex-smoker compared with non-smoker), family history of lung cancer in first degree relative, and use of oral contraceptive for at least a year came out as significant risk factors at 5% level of significance. By multivariate analysis (age-matched), only cigarette smoking (both current and ex-smoker) and family history of lung cancer (first degree) came out as significant risk factors (Table 2).

2. Breast – By bivariate analysis (sex-and age-matched), passive smoking, family history of breast cancer (first degree), consumption of scalding hot food, and increasing age at first pregnancy were significant risk factors, while inverted cigarette smoking, consumption of canned meats, *patis* or *bagoong* and increasing number of pregnancies were significant protective factors. By multivariate analysis family history of breast cancer (first degree), consumption of scalding hot food >5 days/month, and increasing age at first pregnancy were significant risk factors. Inverted cigarette smoking and consumption of *patis* were found to be protective factors (Table 3).

3. Colon-Rectum – By bivariate analysis, exposure to moldy food (≥1/ month), UV sunlight exposure (≥7x/month) and wood dust were significant risk factors. By multivariate analysis, these three factors were also identified as statistically significant but the lower limits of the 95% confidence interval of their odds ratios were very near the null value of 1. Table 4 presents this data.

4. Oral cavity – By bivariate analysis, smoking (current smoker, ex-smoker, passive, inverted), tobacco chewing, betel quid chewing, consumption of scalding hot and salted food (>5 days/month), exposure to pesticides (≥ 1/week), UV sunlight exposure (≥ 7x/month) came out as significant risk factors, while consumption of canned meat (daily to 2x/month), *patis* and *bagoong* (daily to 2x/month) were protective factors. By multivariate analysis, smoking experience (current, ex-, passive, chew, inverted), was a significant risk factor, while use of *bagoong* (daily to 2x/month) and *patis* (daily to 2x/month) were significant protective factors. Betel quid chewing's effect was weaker in the presence of the more significant smoking risk factors. Table 5 shows details.

Discussion

From this case-control study in Filipinos, the possible risk factors (by multivariate analysis) for development of lung, breast, and oral cavity cancers, consistent with literature, are listed in Table 6.

Three factors for colon-rectal cancer were found to be statistically significant but the lower limits of the 95% confidence interval were very near the null value of 1.00.

Lung Cancer

The association between lung cancer and smoking is probably the most intensively investigated relationship in epidemiology and research has provided evidence for the conclusion that smoking causes lung cancer.[1] Compared with continuous smokers, the excess risk sharply decreases in ex-smokers approximately five years after quitting, but a small excess risk persists in long-term quitters throughout life.[1] A positive family history can be linked to cigarette smoking in the family. For passive smoking, the crude OR was 1.42; however, the 95% CI was 0.88-2.28, only giving evidence for a trend towards association.

Breast Cancer

For breast cancer, strong risk factors (OR≥2) reported in the literature are female sex, old age, upper social class, older age at first pregnancy, family history of breast cancer in a first degree relative (but only 2-3% of breast cancer cases have a family link), and premenopausal bilateral breast cancer, previous history of breast cancer, history of fibrocystic disease of the breast, and irradiation of thorax or breast. Other significant risk factors identified in the literature (with ORs < 2) are white race, urban place of residence, unmarried status, nulliparity, small number of children, past-history of ovarian/endometrial cancer, early age at menarche, late age at natural menopause, no oophorectomy, obesity, high alcohol consumption, prolonged oral contraceptive use/ hormone replacement therapy, and mammographic dense breast parenchymal patterns.[5]

Table 1. Age and sex demographics by cancer type

Cancer Site	Group	No.	Age, in years Mean (SD)	Male Sex Number (%)
Lung	Cases	119	59.2 (9.5)	91 (76%)
	Controls	246	54.1 (14.5)	167 (68%)
Colon-rectal	Cases	224	54.2 (13.5)	131 (58%)
	Controls	276	50.8 (13.0)	131 (47%)
Oral Cavity	Cases	176	58.3 (13.3)	90 (51%)
	Controls	317	47.0 (15.8)	120 (38%)
Breast	Cases	297	51.0 (11.4)	0
	Controls	371	41.0 (15.8)	0

In the 1988-1991 case-control study[4] on breast cancer among Filipino women, risk factors identified were a history of benign breast disease (OR=2.51, 95% CI= 1.38-4.57), late age at first pregnancy (95% CI=1.31-15.7) and low fertility (OR=5.83, 95% CI=1.21-28.0). These risk factors are consistent with results of other studies. Other significant factors (some protective) identified were breast feeding (0.57, 0.33-0.98), number of livebirths (0.88, 0.80-0.96), severe dysmenorrhea (0.24, 0.09-0.64), residence in rural areas (2.78, 1.90-4.06), and educational level (1.87, 1.22-2.86). Like the study among Chinese in Taiwan[3], this study indicated no cancer risk associated with menarche, lactation, and menopause. The role of dysmenorrhea as a protective factor is hard to explain, particularly in the absence of other menstrual irregularities depictive of unopposed estrogen inducing susceptibility of the mammary glands to environmental carcinogens.[6]

Studies by the Collaborative Group on Hormonal Factors in Breast Cancer (1996),[7,8] wherein Filipino subjects were included reported the following:

a) Women who were currently using combined oral contraceptives (OCs) or have used them in the last ten years are at a slightly increased risk of having breast cancer diagnosed (current users, RR=1.24, 95% CI=1.15-1.33; 1-4 years after stopping, RR=1.16, 95% CI=1.08-1.23; 5-9 years after stopping, RR=1.07, 95% CI=1.02-1.13),

b) Additional cancers diagnosed tend to be localized to the breast.

c) There was no evidence of an increase in risk of having breast cancer diagnosed 10 or more years after stopping use of OCs (RR=1.01, 95% CI=0.96-1.05), but the cancers diagnosed then were less advanced clinically than cancers diagnosed on patients who have never used OCs;

d) Post-menopausal women were at an increased risk of having breast cancer diagnosed while using hormone replacement therapy (HRT) and in the five years after stopping use of HRT, the relative risk (RR) increases by 2.7% (SD 0.7%) for each year of use. There was no evidence of an increased risk of breast cancer five or more years after stopping use of HRT.

The significant risk factors for breast cancer in this study were similar to those reported in the literature: family history and increasing age at first pregnancy. Oddly, consumption

Table 2. Factors for lung cancer development: age-matched analysis

Suspected Risk Factor	Bivariate Analysis				Adjusted Odds Ratio (95% CI) from multivariate analysis
	Crude Odds Ratio	95% Confidence Interval (CI)			
		Lower Limit	Upper Limit	p-value	
Family history of lung ca - 1st degree	**4.44**	**1.36**	**14.46**	**0.013**	4.29 (1.30 – 14.19)*
Current cigarette smoker	**3.62**	**1.65**	**7.92**	**0.001**	3.56 (1.61-7.86)**
Ex-smoker	**2.50**	**1.14**	**5.49**	**0.022**	2.52 (1.14 – 5.57)***
Chew tobacco	0.41	0.08	1.98	0.264	
Inverted cigarette smoking	0.27	0.03	2.36	0.238	
Passive smoking	1.42	0.88	2.28	0.149	
Betel quid chewing	0.54	0.06	5.24	0.597	
Current drinker, alcohol	1.19	0.56	2.51	0.657	
Ex-drinker, alcohol	1.02	0.47	2.21	0.966	
Oral contraceptive use (> 1/ year)	**4.09**	**1.23**	**13.56**	**0.021**	
Consumption of canned meat (daily - 2x/month)	1.14	0.69	1.89	0.604	
Consumption of fish sauce (patis) (daily - 2x/month)	0.96	0.60	1.55	0.873	
Consumption of shrimp paste (*bagoong)* (daily - 2x/month)	1.00	0.63	1.59	1.000	
Consumption of vegetables (> 1x/week)	1.49	0.70	3.17	0.306	
Consumption of scalding hot food (> 5 days/month)	1.02	0.62	1.66	0.944	
Consumption of preserved food (nitrite-treated) (>5 days/month)	0.66	0.38	1.15	0.142	
Consumption of smoked food (> 5 days/month)	0.86	0.54	1.37	0.532	
Consumption of salted food (> 5 days/month)	0.93	0.54	1.59	0.787	
Exposure to moldy food (> 1/ month)	1.01	0.64	1.61	0.956	
Exposure to pesticide (> 1/week)	0.79	0.28	2.23	0.663	
Vinyl chloride occupational exposure	0.71	0.21	2.38	0.574	
Benzene occupational exposure	0.26	0.06	1.23	0.262	
UV sunlight exposure (> 7x /month)	0.91	0.51	1.63	0.750	
Coal carbonization occupational exposure	1.41	0.29	6.79	0.667	
Wood dust occupational exposure	1.16	0.57	2.38	0.681	

*p-value=0.016; **p-value=0.001; ***p-value= 0.017

Table 3. Factors for breast cancer development: age and sex-matched analysis

Suspected Risk Factor	Bivariate Analysis				Adjusted Odds Ratio (95% CI) from multivariate analysis
	Crude Odds Ratio	95% Confidence Interval (CI)			
		Lower Limit	Upper Limit	p-value	
Family history of breast ca - first degree only	**2.34**	**1.07**	**5.11**	**0.033**	2.95 (1.16 – 7.49)*
Current smoker	0.83	0.49	1.41	0.490	
Ex-smoker	0.57	0.29	1.11	0.096	
Chew tobacco	0.27	0.02	3.06	0.291	
Inverted cigarette smoking	**0.26**	**0.08**	**0.87**	**0.029**	0.21 (0.05 – 0.88)**
Passive smoking	**1.67**	**1.13**	**2.47**	**0.011**	
Betel quid chewing	0.44	0.07	2.68	0.369	
Current drinker, alcohol	1.07	0.69	1.64	0.770	
Ex-drinker, alcohol	0.79	0.42	1.49	0.788	
Canned meat eater (daily - 2x/month	0.66	0.44	0.99	0.044	
Consumption of fish sauce (patis) (daily - 2x/month)	**0.42**	**0.30**	**0.60**	**<0.001**	0.34 (0.22 – 0.51)***
Consumption of shrimp paste (bagoong) (daily - 2x/month)	**0.51**	**0.36**	**0.72**	**<0.001**	
Consumption of vegetables (at least 1x/week)	0.85	0.51	1.43	0.551	
Consumption of scalding hot food (> 5 days/month)	**1.73**	**1.23**	**2.43**	**0.002**	1.52 (1.02 – 2.30)****
Consumption of preserved food (nitrite) (>5 days/month)	1.10	0.77	1.59	0.593	
Consumption of smoked food (>5 days/month)	1.06	0.75	1.49	0.759	
Consumption of salted food (> 5 days/month)	1.42	0.92	2.19	0.117	
Exposure to moldy food (at least monthly)	1.32	0.94	1.85	0.112	
Exposure to pesticide (> 1/week)	0.95	0.40	2.24	0.906	
Vinyl chloride occupational exposure	0.93	0.32	2.71	0.889	
Benzene occupational exposure	2.35	0.50	10.94	0.278	
UV sunlight exposure (> 7x/month)	0.56	0.28	1.11	0.097	
Coal carbonization occupational exposure	1.73	0.25	11.81	0.574	
Wood dust occupational exposure	2.87	0.71	11.58	0.138	
Age at menarche	1.01	0.92	1.10	0.909	
Number of pregnancies	**0.91**	**0.84**	**0.99**	**0.030**	
Age at first pregnancy	**1.06**	**1.02**	**1.10**	**0.005**	1.06 (1.02 – 1.11)*****
Oral contraceptive use (> 1/ year)	1.32	0.85	2.03	0.213	

p-values *0.023; **0.032 ***<0.001; ****0.045 *****0.003

Table 4. Factors for colon-rectum cancer development: age- matched analysis

Suspected Risk Factor	Bivariate Analysis				Adjusted Odds Ratio (95% CI) from multivariate analysis
	Crude Odds Ratio	95% Confidence Interval (CI)			
		Lower Limit	Upper Limit	p-value	
Family history of colorectal cancer – 1st degree only	1.48	0.69	3.16	0.831	
Current smoker	1.44	0.85	2.44	0.178	
Ex-smoker	1.23	0.73	2.07	0.431	
Passive smoking	0.92	0.62	1.36	0.681	
Betel quid chewing	3.36	0.34	33.59	0.303	
Current drinker, alcohol	1.05	0.63	1.76	0.851	
Ex-drinker, alcohol	1.06	0.62	1.80	0.833	
Consumption of canned meat (daily - 2x/month)	1.47	0.98	2.20	0.064	
Consumption fish sauce (patis) user (daily - 2x/month)	1.33	0.92	1.94	0.132	
Consumption of shrimp paste (bagoong) (daily – 2x/month)	1.40	0.97	2.02	0.074	
Consumption of vegetables (> 1x/week)	0.86	0.49	1.49	0.582	
Consumption of scalding hot food (> 5 days/month)	1.07	0.72	1.58	0.752	
Consumption of preserved food (nitrite) (>5 days/month)	1.34	0.87	2.07	0.190	
Consumption of smoked food (>5 days/month)	1.35	0.93	1.96	0.116	
Consumption of salted food (>5 days/month)	0.85	0.55	1.29	0.408	
Exposure to moldy food (> 1/ month)	1.61	1.11	2.35	0.017	2.47 (1.11 – 5.48)*
Pesticide exposure (> 1/week)	1.12	0.42	2.99	0.520	
Vinyl chloride occupational exposure	2.49	0.96	6.47	0.062	
Benzene occupational exposure	2.35	1.00	5.50	0.049	
UV sunlight exposure (> 7x/month)	1.99	1.16	3.39	0.012	1.75 (1.01 – 3.03)**
Coal carbonization occupational exposure	2.17	0.38	12.38	0.384	
Wood dust occupational exposure	2.66	1.21	5.83	0.015	1.48 (1.01 – 2.17)***
Oral contraceptive user (at least a year)	1.42	0.75	2.66	0.278	

p-values: *0.043; **0.045; ***0.027

Table 5. Factors of oral cavity cancer development: age-matched analysis

Suspected Risk Factor	Bivariate Analysis				Adjusted Odds Ratio (95% CI) from multivariate analysis
	Crude Odds Ratio	95% Confidence Interval (CI)			
		Lower Limit	Upper Limit	p-value	
Family history of head & neck cancer – 1st degree only	0.76	0.12	4.80	0.771	
Current smoker	3.12	1.79	5.43	<0.001	1.99 (1.20 – 3.31)*
Ex-smoker	2.26	1.28	4.00	0.005	
Chew tobacco	6.04	1.73	21.07	0.005	5.16 (1.37 – 19.50)**
Inverted cigarette smoker	4.45	1.97	10.04	<0.001	3.22 (1.28 -8.08)***
Passive smoking	3.97	2.32	6.81	<0.001	2.81 (1.57 – 5.06)****
Betel quid chewing	6.94	2.01	23.93	0.002	
Current drinker, alcohol	1.19	0.67	2.11	0.554	
Ex-drinker, alcohol	0.91	0.48	1.74	0.777	
Oral contraceptive use (at least a year)	0.56	0.22	1.42	0.220	
Consumption of canned meat (daily - 2x/month)	0.42	0.26	0.67	<0.001	
Consumption of fish sauce (patis) (daily - 2x/month)	0.24	0.15	0.37	<0.001	0.44 (0.25 – 0.78)*****
Consumption of shrimp paste (bagoong) (daily - 2x/month)	0.26	0.17	0.40	<0.001	0.48 (0.27-0.84)******
Consumption of vegetables (> 1x/week)	0.64	0.30	1.36	0.244	
Consumption of scalding hot food (> 5 days/month)	1.73	1.13	2.65	0.012	
Consumption of preserved food (nitrite) (>5 days/month)	0.69	0.44	1.08	0.107	
Consumption of smoked food (>5 days/month)	1.52	0.95	2.44	0.079	
Consumption of salted food (> 5 days/month)	2.71	1.61	4.56	<0.001	
Exposure to moldy food (> 1/month)	0.69	0.46	1.05	0.085	
Pesticide exposure (> 1/week)	1.64	0.79	3.39	0.185	
Vinyl chloride occupational exposure	1.00	0.24	4.22	0.998	
Benzene occupational exposure	0.69	0.16	2.96	0.618	
UV sunlight exposure (> 7x/month)	2.01	1.23	3.29	0.006	
Wood dust occupational exposure	2.63	0.96	7.20	0.061	

p-value *0.008; **0.015; ***0.013; ****0.001****; *****0.005;******0.01

of scalding hot food (risk factor) and inverted cigarette smoking (protective factor) were also shown to be statistically significant with multivariate analysis. This could be due to interview or questionnaire reliability problem.

Colon-rectum cancer

Only 5% of cases of colon-rectum cancer are inherited.[1] Diet is the most important exogenous causative factor identified so far. A diet that is high in calories and rich in animal fats, usually red meat, and low in vegetables and fiber is associated with an increased risk of colorectal cancer. Alcohol intake and smoking have also been suggested to increase risk. Epidemiological studies indicate a statistical correlation between the increased occurrence of cancer of

Table 6. Identified risk factors for lung, breast and oral cavity cancers

Risk Factors	Cancers
Cigarette smoking, current smoker	Lung, Oral cavity
Cigarette smoking, ex-smoker	Lung
Passive smoking	Oral cavity
Tobacco chewing	Oral cavity
Inverted cigarette smoking	Oral cavity
Family history of cancer site of interest	Lung, Breast
Increasing age at first pregnancy	Breast

the intestinal tract and the frequent consumption of smoked food.[9] In this study, exposure to moldy food, UV light and wood dust came out as statistically significant risk factors by multivariate analysis. Clinical significance may however be questioned due to the fact that the lower limits of the 95% confidence intervals are very near the null value 1. UV light has been studied to be associated with skin cancers and wood dust with nasal cavity cancer. Aflatoxins in moldy food has been associated with liver cancer.[1] These factors have not been reported to be associated with colon-rectal cancer, but were included in this investigation (as environmental risk factors commonly reported in the literature) for all the cancer types studied, including colon-rectal cancer. Wood dust (to which furniture workers are exposed) and aflatoxin can find its way into the colon-rectum. UV light may be a confounding variable found among study participants who were exposed to a great extent to sunlight, like fishermen. However, UV light exposure is hard to measure. In this study, UV light exposure was defined as exposure to sunlight greater than or equal to seven times a month. This may be a weak way to determine the amount of UV exposure.

Oral Cavity

Similar to what was reported in the literature, smoking behavior (specifically current, passive and inverted smoking) were found in this study to be associated with oral cavity cancer.[10,11] Daily to twice a month intake of fish sauce (patis) and shrimp paste (bagoong) consumption were found to be protective factors. Fish sauce was also shown in this study to be a protective factor for the development of breast cancer. These findings have to be further studued since salty food have been identified as cancer risk factors. Current heavy consumption of salted meat (OR=2.3; 1.1-5.2) was associated with a significant 4.7% increased risk of orophayrngeal cancer after adjusting for tobacco smoking and alcohol consumption.[12] Excess cancer risk has also been shown to be associated with high consumption of salt-preserved meat and fish.[13] Consumption of salt added to food and salt-preserved foods have also been investigated mainly in relation to cancers of the stomach, colorectal and nasopharynx.[1] Intake of salt and salted food has been shown to be associated with gastric cancer.[14]

Other factors that need further investigation are high fruit intake and betel quid chewing. High fruit intake significantly decreased risk (OR=.04) with strongest decrease found with fruit juices and citrus fruits.[11,15] Chewing betel quid (with or without tobacco) was also reported to be a risk factor.[16]

Limitations of this study

Being a case-control study, there are methodological issues that are inherent in this design. Results should be validated using a prospective study design. The questionnaire and techniques used in the interviews should be further refined to minimize bias and improve reliability in determining exposure to certain risk factors such as diet and other lifestyle factors which are inherently hard to measure. The role of fish oil and shrimp paste consumption in cancer development, for example has to be further investigated with more refined measurement instruments.

This study was not able to study the role of certain genetic markers in cancer development. This is being addressed by another study by the Philippine Cancer Genetics Study group. For example, the association of polymorphisms, K-ras and p53 as biomarkers in these 4 primary sites of cancer is currently being investigated and will be reported in another paper.

Conclusions and Recommendations

Except for family history of cancer, all of the above identified risk factors for cancers of the lung, breast colon-rectum, and oral cavity are preventable. Proper diet and lifestyle, avoidance of cigarette smoking, tobacco and betel quid usage, and environmental safety in the workplace are key factors in primary prevention of cancer. In all aspects of primary and secondary prevention of cancer among the populace, public awareness campaign and continuing healthcare provider education should be incorporated in any health program.

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