Published OnlineFirst May 1, 2016; DOI: 10.1158/1055-9965.EPI-15-0626

Research Article

Cancer Epidemiology, Biomarkers & Prevention

Cancer Mortality Risks from Long-term Exposure to Ambient Fine Particle

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Abstract

Background: Few studies have assessed long-term effects of particulate matter (PM) with aerodynamic diameter < 2.5 μm ($PM_{2.5}$) on mortality for causes of cancer other than the lung; we assessed the effects on multiple causes. In Hong Kong, most people live and work in urban or suburban areas with high-rise buildings. This facilitates the estimation of $PM_{2.5}$ exposure of individuals, taking into account the height of residence above ground level for assessment of the long-term health effects with sufficient statistical power.

Methods: We recruited 66,820 persons who were ≥65 in 1998 to 2001 and followed up for mortality outcomes until 2011. Annual concentrations of PM at their residential addresses were estimated using $PM_{2.5}$ concentrations measured at fixed-site monitors, horizontal–vertical locations, and satellite data. We used Cox regression model to assess the HR of mortality for cancer per 10 $\mu g/m^3$ increase of $PM_{2.5}$.

Results: $PM_{2.5}$ was associated with increased risk of mortality for all causes of cancer [HR, 1.22 (95% CI, 1.11–1.34)] and for specific cause of cancer in upper digestive tract [1.42 (1.06–1.89)], digestive accessory organs [1.35 (1.06–1.71)] in all subjects; breast [1.80 (1.26–2.55)] in females; and lung [1.36 (1.05–1.77)] in males.

Conclusions: Long-term exposures to $PM_{2.5}$ are associated with elevated risks of cancer in various organs.

Impact: This study is particularly timely in China, where compelling evidence is needed to support the pollution control policy to ameliorate the health damages associated with economic growth. *Cancer Epidemiol Biomarkers Prev; 25(5); 839–45. ©2016 AACR.*

Introduction

Emissions from transportation and power generation are the major sources of carcinogenic hydrocarbons and heavy metals in particulate matter (PM; ref.1). Long-term exposure to PM has been associated with mortality mainly from cardiopulmonary causes and lung cancer, but there have been few studies showing an association with mortality from other cancers (2–11). Two main biologic mechanisms to explain PM-associated cancer mortality have been postulated: first, an effect of oxidative stress induced by PM on epithelial cells to produce reactive oxygen species that can damage DNA, proteins, and lipids (12); and second, an effect of inflammation induced directly or indirectly by PM, leading to the production of chemokines and cytokines to trigger angiogenesis, allowing epithelial invasion of metastatic tumor cells and then survival of the invading malignant cells in distant organs (13). It is plausible that PM-associated carcinogenic risk could appear in organs other than the nasal cavities and lungs, but there are few epidemiologic studies addressing the postulation. This was a prospective cohort study; the methods before taking into account of floor level in estimation of the exposure and results on mortality for all-natural and cardio-respiratory causes have been published (14). In this study, we assessed the associations of mortality for various causes of cancer with long-term exposure to PM.

Materials and Methods

Subjects and individual information

A total of 18 Elderly Health Centres were established to deliver health examinations and primary care services for older adults in Hong Kong by the Elderly Health Service of the Department of Health of the Government of the Hong Kong Special Administrative Region that aimed to promote the health of elderly population in each district and to enhance self-care ability so as to minimize illness and disability. Nurses and doctors of the Elderly Health Centres that are located in each of the 18 districts in Hong Kong provided health assessment, using standardized and structured interviews, and comprehensive clinical examinations. Information on sociodemographic, lifestyles, and disease history was collected as described in a previous study using the data collected by the Elderly Health Service (15). This study covered all 66,820 enrollees from July 1998 to December 2001, who were recruited on voluntary basis, accounting for 9% of the 65 or older population at the baseline year (the sampling fractions ranging from 6.6%–17.5% of the population older than 65 years of age in each

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

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doi: 10.1158/1055-9965.EPI-15-0626

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district; ref.16). The protocol was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster and the ethics committee of the Department of Health.

Follow-up

Vital status and causes of death were ascertained by record linkage to death registration in Hong Kong using the unique Hong Kong identity card number. The last date of follow-up or censor date was December 31, 2011. Causes of death were routinely coded using International Classification of Diseases (ICD) 9th Revision before 2001 and 10th Revision in or after 2001. Most of the Hong Kong residents died in hospital, ensuring accurate ascertainment of the cause of death. Those whose vital status could not be determined were assumed to be alive.

Mortality outcomes

The cause of death was coded by both ICD-9 and ICD-10 over the study period from 1998 and was based on the underlying cause of death according to the underlying etiology or injury that initiated the chain of morbid events leading directly to death. The mortality causes considered in this study were subcategories of cancer, which accounted for at least 100 deaths. They were: all malignant neoplasms or cancers ICD10:C00-C99 (or ICD9:140-209). Subcategories of cancers included were: all digestive organs C15-C26 (150–159) which were subdivided into (i) upper digestive tract C15-16 (150–151), including esophagus and stomach, (ii) lower digestive tract C17-21 (152–154), including small intestine, colon, rectum, appendix, and anus, and (iii) accessory organs C22-25 (155–157), including liver, gall bladder, and pancreas; lung, including trachea C33-C34 (162); breast C50 (174); female genital C51-C58 (179–184); male genital C60-C63 (185–187); urinary C64-C68 (188–189); and lymphohematopoietic C81-C96 (200–209). To assess the specificity, we assessed the causes of poisoning and injuries (S00–Y98) mortality, which was considered to be unrelated to PM exposure.

Individual, ecological, and environmental covariates

On the basis of the data from a standardized questionnaire, we included individual covariates of age, gender, body mass index (BMI), smoking status, exercise frequency, education level, and personal monthly expenditure. On the basis of census statistics in 197 land areas, by the Tertiary Planning Units (16), we included ecological covariates in percentage of older subjects (aged 65+), percentage with tertiary education, and monthly domestic household income. From 18 districts of Hong Kong, we included environmental covariates in percentage of smokers (aged 15+) for the indication of exposure to environmental tobacco smoke in each year. On the basis of *ad hoc* survey, we included ground radon levels ($kBqm^{-3}$) in 1×1 km grid of a data map (17–19).

Exposure estimation model

We calculated annual mean concentrations ($\mu g/m^3$) of PM with aerodynamic diameter < 2.5 μm ($PM_{2.5}$) based on the data from 5 stations run by the Environmental Protection Department, which has monitored hourly concentrations of the pollutants by tapered element oscillating microbalance from 1998 until 2011. In all the locations, we obtained their geospatial height above the mean sea level and the satellite information in 1×1 km grids of surface extinction coefficients (20–22). Then, we fitted regression models to estimate $PM_{2.5}$ concentrations using surface extinction coefficients and inverse geospatial height (i.e., 1/height) of the residential location above the mean sea level as independent variables.

We geocoded all residential addresses of the subjects and matched them with the surface extinction coefficients data. We calculated the vertical height of each address based on the floor number. Using the abovementioned exposure model, we estimated the annual mean concentrations of $PM_{2.5}$ in each residential location. We then compared the estimates with the results independently obtained from a deterministic model based on street canyon geometry, traffic census, air pollution, and meteorologic data for an area where the data were available (23).

Statistical analysis

For each organ-specific cancer mortality dataset, we used Cox proportional hazards model to estimate the HR of mortality ($n = 60{,}273$) for every 10 $\mu g/m^3$ increase of long-term exposure to $PM_{2.5}$ concentration, with adjustment for individual, ecological, and environmental covariates after excluding subjects (9.8%) with missing data in any covariates that were mentioned previously. We used time-on-study from the baseline as timescale and the estimated exposure in the subjects' recruitment year (between 1998 and 2001) to represent long-term exposure. To control for competing diseases and to assure detection of long-term associations, we excluded deaths due to other causes and deaths that occurred within 3 years from the baseline year, respectively. We stratified the data by ever and never smoker and tested for the difference by an interaction term in the model, respectively, for male and female. We performed the sensitivity analysis by excluding height of address from sea level in the exposure estimation, by using current annual mean $PM_{2.5}$ as time-varying variable in the Cox model, and by competing risks model instead of excluding deaths from competing causes (24) or by excluding subjects with self-reported preexisting respiratory and cardiometabolic

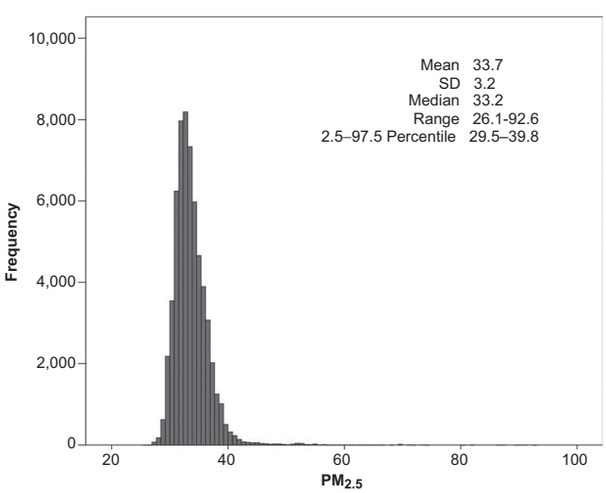

Figure 1.
Distribution of $PM_{2.5}$ ($\mu g/m^3$). The figure depicts the frequency of subjects (*y*-axis) in each class interval (1 $\mu g/m^3$ of $PM_{2.5}$) against $PM_{2.5}$ concentration in $\mu g/m^3$ units (*x*-axis).

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Published OnlineFirst May 1, 2016; DOI: 10.1158/1055-9965.EPI-15-0626

Table 1. HRs adjusted for individual, ecological, and environmental covariates for all cancer mortality due to long-term exposure to $PM_{2.5}$

Characteristics		HR (95% CI)	Number of deaths per 1,000 person-years
Per 10 μg/m^3 increase of $PM_{2.5}$			
Mean ± SD: 33.7 ± 3.2; IQR: 3.3; median (range): 33.2 (26.1–92.6)		1.22 (1.11–1.34)	
Individual:			
Age (year)		1.09 (1.09–1.10)	
Gender	Male as ref.		10.8
	Female	0.68 (0.63–0.74)	6.3
BMI quartiles	Q2–Q3 (21.6–26.3) as ref.		7.5
	Q1 (<21.6)	1.09 (1.02–1.18)	9.3
	Q4 (>26.3)	1.05 (0.98–1.13)	7.1
Smoking	Never-smoked as ref.		6.1
	Quitted	1.49 (1.37–1.61)	10.9
	Current	2.33 (2.13–2.54)	14.2
Exercise (days/week)		0.98 (0.96–1.01)	
Education	Secondary or above as ref.		7.5
	Primary	1.07 (0.98–1.16)	8.5
	Below primary	1.08 (0.99–1.19)	7.4
Monthly expenditure (US$)	<128	0.97 (0.87–1.09)	7.3
	128–384	1.07 (0.98–1.16)	8.0
	≥385 as ref.		7.4
Ecological:			
Age ≥ 65		0.99 (0.98–1.00)	
Education as tertiary level		0.99 (0.98–1.00)	
Income/month ≥ US $1,923		1.00 (1.00–1.01)	
Environmental:			
Tobacco smoke (as % of smokers)		1.21 (1.05–1.40)	
Radon (kBqm^{-3})	0–40 as ref.		8.1
	41–100	1.06 (0.97–1.15)	7.6
	≥101	1.08 (0.98–1.20)	8.0

NOTE: 47,594 subjects were included in the model. 4,531 of them died of cancers.
Abbreviations: IQR, interquartile range; ref., reference.

diseases at baseline. Death records were the primary follow-up information in this study (with average of 10.3 years and range 0–13 years of follow-up), but those that might have been lost to follow-up due to a change in address or migration were not traceable. Among the nonmissing records until the last follow-up year, there were 16% of them who did not appear in any formal records of adverse health events or in any questionnaire interviews in the last 3 years, which might be due to loss to follow-up. Therefore, we also performed the sensitivity analysis by excluding these 16% potential loss to follow-up subjects from the analysis. Further sensitivity analyses were performed to exclude deaths within 5 or 7 years, subjects who had moved during the follow-up period or had been hospitalized during 1998 to 2000, to take account of diseases that may take longer than 3 years for the incubation period, the effect of moving address and the effect of mixing with prevalent cases, respectively. Cox models were performed using the command PHREG in Statistical Analysis System 9.2. We plotted the relationship between $PM_{2.5}$ and deaths from all cancers using the natural splines command COXPH in R 3.0.1 with two degrees of freedom. As a sensitivity analysis, we also used models with random effects set at the intercepts to take account of possible intradistrict correlations (25, 26).

Results

In the exposure models for $PM_{2.5}$ ($R^2 = 0.47$), both inverse height ($P < 0.001$) and surface extinction coefficients ($P < 0.01$)

Table 2. HRs for mortality of all natural causes and specific cancers per 10 μg/m^3 of $PM_{2.5}$

ICD10	Causes of mortality	*n*[a]	HR[b] (95% CI)	*P*
A00-R99	All natural causes	14,398	1.13 (1.08–1.19)	<0.001
C00-C97	All malignant	4,531	1.22 (1.11–1.34)	<0.001
C15-26	All digestive organs	1,734	1.22 (1.05–1.42)	0.01
C15-16	Upper digestive tract	323	1.42 (1.06–1.89)	0.02
C17-21	Lower digestive tract	719	1.01 (0.79–1.30)	0.91
C22-25	Accessory organs	676	1.35 (1.06–1.71)	0.01
C33-34	Lung	1,408	1.14 (0.96–1.36)	0.14
C50	Breast	111	1.80 (1.26–2.55)	0.001
C51-58	Female genital	138	1.73 (1.17–2.54)	0.006
C60-63	Male genital	143	1.02 (0.51–2.04)	0.96
C64-68	Urinary	155	0.98 (0.58–1.64)	0.93
C81-96	Lymphohematopoietic	310	1.29 (0.86–1.95)	0.21

[a]*n* = number of deceased subjects.
[b]HRs were adjusted for all covariates as in Table 1.

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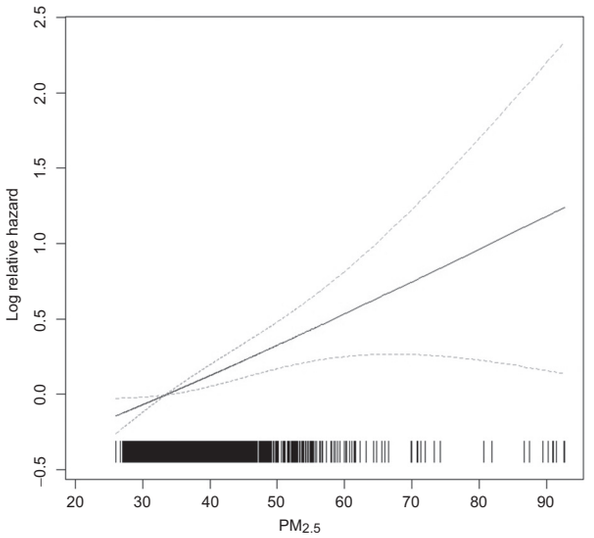

Figure 2.
The pattern of association between all-cancer mortality risk and long-term exposure to $PM_{2.5}$ ($\mu g/m^3$). Solid line (95% CI: dashed line) based on fully adjusted model in Table 1, with natural spline on 2 degrees of freedom. The marks above the *x*-axis show the measurements with the crowdedness, indicating the distribution of $PM_{2.5}$ concentration.

were significant predictors. Comparison of the empirically estimated PM concentrations with those estimated from deterministic model for street canyon yielded good validation measures (Supplementary Table S1). The estimated $PM_{2.5}$ mean concentration (2.5–97.5 percentile) in the baseline year at individual residential locations was 33.7 (29.5–39.8) $\mu g/m^3$ (Fig. 1).

Subjects who were exposed to cleaner air quality tended to be younger, had a higher BMI and were never-smokers, frequent exercisers, better educated, lower in personal expenditure, and were located in areas with fewer older people, higher levels of education, higher income, and higher radon levels (all $P < 0.01$). Significant covariates identified in the Cox regression model of cancer mortality were older, male, underweight, ever smoked, and less educated and lived in a community with younger, less educated, and with more smoking subjects (Table 1).

$PM_{2.5}$ was associated with all-cancer mortality [HR, 1.22; 95% confidence interval (CI), 1.11–1.34] as well as cause-specific cancer mortality, including all digestive organs (HR, 1.22; 95% CI, 1.05–1.42), upper digestive tract (HR, 1.42; 95% CI, 1.06–1.89), and accessory digestive organs (HR, 1.35; 95% CI, 1.06–1.71). In female, the associations were shown in breast (HR, 1.80; 95% CI, 1.26–2.55) and genital organs (HR, 1.73; 95% CI, 1.17–2.54; Table 2). $PM_{2.5}$ was not significantly ($P > 0.05$) associated with external causes. A linear concentration–response relationship between $PM_{2.5}$ and all-cancer mortality was shown (Fig. 2).

In the stratified analysis, $PM_{2.5}$ (per 10 $\mu g/m^3$ increase) was associated with mortality due to lung cancers (HR, 1.39; 95% CI, 1.05–1.77) among male subgroup (Table 3). The HRs in the sensitivity analyses (Table 4) were consistent to those in the main analyses in terms of magnitude and direction of deviation from the null effect estimate.

Discussion

We showed that in older people, cancer mortality risks were associated with long-term exposure to particulate air pollutants in a typical Asian city, Hong Kong, where the people dwell mainly in high-rise buildings. We demonstrated carcinogenic risks of $PM_{2.5}$ in multiple organs and tissues using the approach for a single prospective cohort. There are few studies in the literature comparing $PM_{2.5}$ associations on cancer mortality among different organs or tissues. We found stronger associations with $PM_{2.5}$ in

Table 3. Stratification analysis: HRs for mortality of cancer per 10 $\mu g/m^3$ of $PM_{2.5}$ in male and female subjects

(i) Male								
	All subjects			Never smoker		Ever smoker		Interaction
Causes of mortality	*n*	HR (95% CI)	*P*	*n*	HR (95% CI)	*n*	HR (95% CI)	*P*
All malignant	2,043	1.31 (1.13–1.51)	<0.001	553	1.23 (0.90–1.67)	1,490	1.33 (1.13–1.56)	0.75
All digestive organs	791	1.29 (1.01–1.65)	0.04	261	1.23 (0.83–1.83)	530	1.32 (0.98–1.78)	0.94
Upper digestive tract	176	1.46 (0.98–2.18)	0.06	54	1.49 (0.79–2.81)	122	1.44 (0.88–2.35)	0.31
Lower digestive tract	311	1.21 (0.81–1.81)	0.35	105	1.13 (0.61–2.07)	206	1.23 (0.76–2.01)	0.46
Accessory organs	298	1.28 (0.83–1.96)	0.26	101	1.09 (0.55–2.18)	197	1.37 (0.81–2.32)	0.98
Lung	677	1.36 (1.05–1.77)	0.02	100	1.19 (0.52–2.74)	577	1.37 (1.05–1.78)	0.41
Male genital	143	1.02 (0.51–2.04)	0.96	64	0.75 (0.22–2.61)	79	1.16 (0.49–2.78)	0.86
Urinary	87	1.03 (0.48–2.24)	0.93	22	0.41 (0.04–3.84)	65	1.14 (0.56–2.35)	0.23
Lymphohematopoietic	124	1.65 (0.93–2.94)	0.09	49	0.97 (0.36–2.63)	75	2.05 (1.05–4.02)	0.59

(ii) Female								
	All subjects			Never smoker		Ever smoker		Interaction
Causes of mortality	*n*	HR (95% CI)	*P*	*n*	HR (95% CI)	*n*	HR (95% CI)	*P*
All malignant	2,488	1.17 (1.03–1.32)	0.02	2,047	1.17 (1.02–1.34)	441	1.12 (0.82–1.52)	0.38
All digestive organs	943	1.16 (0.96–1.41)	0.13	821	1.17 (0.96–1.44)	122	1.01 (0.59–1.71)	0.26
Upper digestive tract	147	1.37 (0.91–2.05)	0.13	127	1.35 (0.89–2.04)	20	1.25 (0.36–4.27)	0.52
Lower digestive tract	408	0.88 (0.64–1.23)	0.46	354	0.91 (0.64–1.28)	54	0.72 (0.26–2.02)	0.63
Accessory organs	378	1.37 (1.05–1.80)	0.02	332	1.36 (1.01–1.84)	46	1.39 (0.79–2.45)	0.58
Lung	731	0.99 (0.77–1.27)	0.92	523	1.01 (0.76–1.36)	208	0.95 (0.61–1.47)	0.99
Breast	111	1.80 (1.26–2.55)	0.001	99	1.66 (1.10–2.50)	12	7.14 (2.01–25.4)	0.10
Female genital	138	1.73 (1.17–2.54)	0.006	126	1.65 (1.07–2.55)	12	2.48 (1.09–5.61)	0.53
Urinary	68	0.89 (0.45–1.79)	0.75	53	1.03 (0.54–1.96)	15	0.35 (0.03–4.18)	0.30
Lymphohematopoietic	186	1.12 (0.62–2.02)	0.70	161	1.17 (0.62–2.19)	25	0.84 (0.26–2.75)	0.99

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Table 4. Sensitivity analyses: HRs for mortality of all cancers per 10 μg/m^3 of $PM_{2.5}$

Sensitivity	*n*	HR (95% CI)	*P*
Without using geospatial height in exposure estimation	4,546	1.20 (1.06–1.36)	0.005
Time-varying annual mean exposure instead of baseline year exposure	4,514	1.21 (1.10–1.33)	<0.001
Without control of competing diseases	4,531	1.21 (1.10–1.33)	<0.001
Exclusion of subjects as potential loss to follow-up	4,531	1.23 (1.12–1.35)	<0.001
Exclusion of deaths for the first 5 years	3,697	1.23 (1.11–1.37)	<0.001
Exclusion of deaths for the first 7 years	2,706	1.14 (1.04–1.25)	0.015
Exclusion of subjects who had moved during the follow-up period	4,192	1.22 (1.11–1.35)	<0.001
Exclusion of subjects who had hospitalization record in 1998–2000	2,687	1.25 (1.12–1.41)	<0.001
Exclusion of subjects with self-reported preexisting respiratory or cardiometabolic diseases at baseline	2,582	1.20 (1.05–1.37)	0.006
Adjustment for alcohol intake			
All malignant	4,531	1.22 (1.11–1.34)	<0.001
All digestive organs	1,734	1.22 (1.05–1.42)	0.01
Random effects with adjustment of autocorrelation at planning areas (i.e., Tertiary Planning Units)	4,531	1.22 (1.11–1.34)	<0.001
Competing risks	4,531	1.14 (1.04–1.25)	0.007

the upper digestive tract and accessory organs and breast than among all-cancer or all-digestive organs. Although most of our findings on specific cancers were not reported in the American Cancer Society study, our observations are consistent with the American Cancer Society study in a way that the excess risks of specific causes were larger than those of less specific causes (9). Our HRs per 10 μg/m^3 $PM_{2.5}$ for female genital cancer and for breast cancer were about 40% to 50% higher than the reported relative risk (1.20 and 1.19, respectively) in an ecological study of all ages in Taiwan (27, 28). When compared with the American Cancer Society study, our HR per 10 μg/m^3 $PM_{2.5}$ for all-digestive organs and for male lung cancer was fairly similar to their respective HR of 1.20 and 1.43, adjusted for individual covariates and components of social factors (9).

A hypothesis for an explanation at the molecular level of the carcinogenic effects of PM could be in terms of defects in DNA repair function and replication (29). Effects of oxidative stress due to air pollution have also been shown in biomarker studies (30). However, pathologic explanations for specific cancer mortality are rare. For digestive systems, the hypothesized mechanisms include inflammations of gut lining epithelial cells, following ingestion, alterations in immune response, and effects on gut microbiota (31). These hypotheses may be connected to aerosolized pollutants, which are trapped by mucus and swallowed, eventually passing through the whole digestive tract and affecting the epithelial cells and the gut microbiota. A large-scale European case–control study of household wood burning on esophageal cancer (32) and an ecological Spanish study of industrial metallic aerosols on gallbladder and pancreas cancers have also indicated similar associations of air pollutants with cancer of the upper digestive tract and accessory organs (33).

A human experimental study on metal species in thyroid cancer has hypothesized environmental contamination as a possible factor in explaining the thyroid pathology (34). Although the evidence is still insufficient, the literature has given some support to our findings on the PM-related cancer risks on multiple sites, including digestive system, lung, breasts, genital organs, and lymphohematopoietic tissues.

Most studies of the long-term associations of PM estimated proxy exposure of individuals at the region of residence, either using geospatial/dispersion modeling or satellite information (5, 9, 35–38). However, the estimation of chronic health associations of PM using intraregion spatial variation in this study has resulted in similar HRs to those studies relying on contrasts of multiple region-wide average exposures. The smaller estimates in the latter were likely due to the greater exposure measurement errors, which led to underestimation of the pollution-related health burden (9). A California study showed that associations within cities are similar as between cities, and the difference in exposure metrics had little impact on the risk estimates for $PM_{2.5}$ (39). We found that there were no differences between estimates before and after controlling for intra-district correlations with random effect modeling. This result was supported by another U.S. study on incidence of cardiovascular events, incorporating a random effect term for between-city and within-city effects (40).

There were limitations in this study. First, we did not address the associations of multipollutant exposure, indoor air pollution, chemical and physical size components of $PM_{2.5}$. The roles of $PM_{2.5}$ cannot be disentangled from the other environmental pollutants. Second, we did not assess the contribution of genetic factors, metastasis, nor cancer-inhibitory inflammation mechanism for the association, and because of that we were not able to determine the effects of PM on susceptible groups and on cancer development (13). Third, the short period of the study, which does not allow the assessment of health outcomes with long latency period, is another limitation. However, the participants could have already been living in the same address before enrollment, as the 5-year moving rates in the older population were consistent and less than 15% in the past 10 to 15 years (41); only 9.3% of the subjects were found not residing in the same address during the follow-up of around 10 years, and the estimates were robust to exclusion of movers from the analysis. Fourth, most of the subjects (93%) were retired or not working anymore. Yet, their employment history was not known, and any previous occupational exposure was not accounted for. Fifth, the daily activities of the subjects were not assessed in details by questionnaires. However, in our sensitivity analysis, using annual mean exposure at the year of comparison in model should have taken account of this. Outdoor activities (e.g., travelling to other parts of the city) or indoor activities (such as the use of air purifiers), which would affect the exposure level of $PM_{2.5}$, were not adjusted for. Further studies to take these into account are needed. Sixth, stage of cancer at diagnosis was not available in our data, which may affect the choice of treatment method and hence survival from premature death (42). However, as the trends of PM in different geographic areas were stable over the study period, the effect estimates may not be affected substantially.

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Published OnlineFirst May 1, 2016; DOI: 10.1158/1055-9965.EPI-15-0626

Last but not the least, selection bias may be an issue due to voluntary nature in the subject recruitment. Volunteers who were more aware of the "new" provision of elderly health service by the government could tend to be more conscious in seeking health care service, which would potentially lead to underestimation of the risk of PM in this study.

For older people who dwell in a city with a dense population and high-rise buildings in Asia, long-term exposures to particulate air pollutants are associated with mortality from all cancers combined with a linear concentration–response relationship. Associations were also found between $PM_{2.5}$ and various specific cancers, including cancer in lung, all digestive organs, breasts, and genital organs. The magnitudes of risks are comparable with those of other similar studies, providing further evidence to strengthen causality and support health economic assessments of cancer-related deaths attributable to air pollution.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: C.M. Wong, H.K. Lai, G.N. Thomas, J.G. Ayres, S.Y. Lee, T.H. Lam, T.Q. Thach

Development of methodology: C.M. Wong, H. Tsang, H.K. Lai, S.Y. Lee, T.Q. Thach

Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): C.M. Wong, S.Y. Lee

Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): C.M. Wong, H. Tsang, H.K. Lai, K.B. Lam, K.P. Chan, J.G. Ayres, T.Q. Thach

Writing, review, and/or revision of the manuscript: C.M. Wong, H. Tsang, H.K. Lai, G.N. Thomas, K.B. Lam, J.G. Ayres, S.Y. Lee, T.H. Lam, T.Q. Thach

Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): C.M. Wong, H. Tsang, Q. Zheng, S.Y. Lee, T.H. Lam, T.Q. Thach

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Acknowledgments

The authors thank the Hong Kong Special Administration Region departments, including the Department of Health (Elderly Health Services) for cohort data, Census and Statistics Department for mortality data, and Environmental Protection Department for $PM_{2.5}$ data. The authors also thank The Hong Kong University of Science and Technology for satellite information and Department of Geography in The University of Hong Kong for geocoding, and Prof. K.K. Cheng of the University of Birmingham, United Kingdom, for valuable comments.

Grant Support

C.M. Wong had been awarded the Wellcome Trust (#094330/Z10/Z). H. Tsang, H.K. Lai, G.N. Thomas, K.B. Lam, K.P. Chan, and Q.S. Zheng received the above mentioned grant.

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Received June 16, 2015; revised February 22, 2016; accepted February 22, 2016; published OnlineFirst April 29, 2016.

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Cancer Epidemiol Biomarkers Prev 2016;25:839-845. Published OnlineFirst May 1, 2016.

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