Cancer risk from exposure to particulate matter and ozone according to obesity and health-related behaviors: A nationwide population-based cross-sectional study

Kyoung Jin Kim, Jinyoung Shin, Jaekyung Choi

Department of Family Medicine, Konkuk University School of Medicine, Konkuk University Medical Center, Seoul, South Korea

Running title: Particulate matter, ozone and cancer risk

Keywords: Air pollution; Neoplasms; Obesity; Smoking; Exercise; Alcohol drinking

Corresponding author: Jinyoung Shin

Department of Family Medicine, Konkuk University School of Medicine, Konkuk University Medical Center, 120-1 Neungdong-ro, Gwangjin-gu, Seoul 05030, South Korea

Tel: +82-2-2030-7698; Fax: +82-2-2030-7749; E-mail: jyshin@kuh.ac.kr

Conflict of Interest

The authors declare that they have no conflict of interest.

Words: 2,840

Tables: 3

Figures: 1

E-mail address

Kyoung Jin Kim: jjin1202@gmail.com

Jinyoung Shin: jyshin@kuh.ac.kr

Jaekyung Choi: cjk@kuh.ac.kr

Abstract

Background: There is little evidence of an association between cancer risk and long-term exposure to ambient particulate matter <10 μm (PM_{10}) and ozone (O_3) according to obesity and health-related behaviors.

Methods: In the 2012 Korean Community Health Survey, survey data on socioeconomic characteristics, health-related behaviors, and previous cancer history were collected from 100,867 participants. Daily average concentrations of PM_{10} and O_3 (2003-2012) were obtained from the Korean Air Pollutants Emission Service. The cancer risks for interquartile increases in PM_{10} and O_3 were evaluated using multiple logistic regression and were stratified by age, sex, obesity, and health-related behaviors.

Results: Increased cancer risk was found among obese subjects aged ≥50 years after adjusting for confounding factors (PM_{10}: ≥60 years: odds ratio [OR]: 1.34, 95% confidence interval [CI]: 1.03–1.74; 50–60 years: 1.40, 1.00–1.96; O_3: ≥60 years: 1.12, 1.04–1.20; 50–60 years: 1.20, 1.08–1.33). However, we did not observe similar trends in the non-obese subjects. Among obese subjects aged ≥50 who had been exposed to PM_{10}, men, ever smokers, and inactive subjects were at increased cancer risk. Regarding O_3, the cancer risk was significantly higher among obese adults >50 years old, regardless of sex or health-related behaviors.

Conclusions: Long-term exposure to PM_{10} and O_3 was found to increase cancer risk. In particular, the risk differed according to obesity status, age, sex, and health-related behaviors.

Impact: The effect of air pollution on cancer risk was compounded by obesity, smoking, and physical inactivity among subjects over 50 years old**.**

Introduction

In 2013, the International Agency for Research on Cancer classified ambient air pollution as a human carcinogen (1). The air quality standards defined by the World Health Organization (WHO) announced that particulate matter (PM) and ozone (O_3) were the most harmful pollutants in 2006 (2). Long-term PM exposure increases mortality from diseased trachea or bronchus and lung cancer (3-5). Although less evidence is available to evaluate associations between air pollutants and some other cancers, cancer of the bladder (6), liver (7), prostate (8), cervix (9), and pancreas (10) has all been shown to have positive associations with air pollution exposure. In contrast, two studies found no association between air pollution and breast cancer (11,12).

Weight and lifestyle factors may have an influence on the effects of long-term exposure to air pollution, resulting in a nonlinear relationship with cancer mortality. In one recent study, current smoking and alcohol consumption were positively associated with air pollution, while physical activity and overweight status were negatively associated with air pollution (13). Ever smokers exhibited increased cancer mortality from PM exposure, while never smokers did not (14). In a Canadian case-control study examining over 20 years of PM exposure, the incidence of lung cancer was increased in men, but no consistent patterns according to smoking status or education were observed (4). Therefore, a known risk factor-based approach with a focus on clustered risk factors is needed to understand the biological mechanisms that underlie the associations between air pollutant exposure and cancer risk.

O_3 is a secondary pollutant caused by photochemical reactions. The toxicological effects of O_3 result from inflammatory response, oxidative stress, and tissue injury (15). Previous study explored the carcinogenic influence of O_3 on microorganisms, plants, and cell lines in vitro (16), and showed some evidence linking O_3 exposure and cancer development in experimental studies (17). However, the effect of exposure to O_3 on lung cancer-related mortality was not significant in a 20-year Canadian study (18). Moreover, few studies have addressed the association between exposure of O_3 and cancer considering individual risk factors. As most previous studies were carried out in Western populations, differences in race, lifestyle, air-pollutant concentration, and exposure duration may have affected the results.

The aim of this study was to investigate the association between long-term exposure to PM <10 μm (PM_{10}) and O_3 and cancer risk according to obesity status, age, sex, and health-related behaviors in a nationwide population-based cross-sectional study.

Materials and Methods

Study participants

We evaluated data from the 2012 Korean Community Health Survey (KCHS), which has been conducted annually by the Korea Centers for Disease Control and Prevention since 2003. Total 228,921 participants aged 19 or older were enrolled in approximately 900 participants per unit, with units representing 254 communities, including 16 different metropolitan areas and provinces. The KCHS was performed between August and October via computer-assisted personal interviews. The KCHS had public confidence to represent the entire characteristics of Korean population (19). We selected 100,867 participants who had lived at the same residence for ≥10 years, after matching participant residence codes with location of surveillance stations for PM_{10} and O_3.

The institutional review board (IRB) at the Korean Centers for Disease Control and Prevention approved the study protocol, and all of the participants provided written informed consent. The IRB at Konkuk University Medical Center also approved this study (IRB File Number: KUH1230027).

Air pollutant variables

We obtained the average concentrations of hourly measured PM_{10} and O_3 at 268 nationwide surveillance stations from the Korean Air Pollutants Emission Service of the National Institute of Environmental Research. The surveillance stations located in the residential area (**Figure S1**). We calculated the interquartile ranges of the yearly average concentrations for the period of 2003–2012. PM_{10} was measured using beta-ray attenuation (PM-711D; DONGIL GREENSYS, Seoul, Korea). O_3 was measured using ultraviolet photometry (202; TOTAL ENGINEERING CO., LTD, Gyeonggi-do, Korea). These air pollutant measurements followed the standard reference protocol from the Korean Air Pollutants Emission Service (20). We obtained meteorological data from the National Meteorological Office (**Table S1**).

Other variables

The KCHS surveyed socioeconomic parameters, health-related behaviors, and medical history including cancer, hypertension, diabetes mellitus, dyslipidemia, stroke, myocardial infarction, ischemic heart disease, and asthma. Cancer was limited to medical diagnosis regardless of cancer type. Obesity was defined as body mass index (BMI) >25. We categorized patients as never-smokers and ever-smokers, which included former smokers and current smokers. We categorized patients as never-drinkers or drinkers by a drinking frequency of at least one drink per week. We defined physical activity by intensity and frequency, separating patients into an active group and an inactive group. The active group performed moderately intense activity more than three times per week or vigorous activity more than one time per week. Patients who did not meet these criteria were categorized into the inactive group. We divided subjects into three age groups: A1 < 50 years, 50 ≤ A2 <60 years, and A3 ≥ 60 years. We also obtained the following demographic information: years of education (< 9, ≥ 9); marital status (married/with partner or divorced/widowed/unmarried); household income (<1,000,000 won/month or ≥1,000,000 won/month); and place of residence (rural or urban). We excluded participants who had lived at their residence for <10 years and then divided length of residence into three groups: 10 ≤ T1< 15 years, 15 ≤ T2 < 20 years, and T3 ≥ 20 years.

Statistical analyses

Continuous variables are presented as means with standard error, and categorical variables are presented as percentages. We performed univariate analyses to determine the associations between cancer diagnosis and variables. We evaluated the odds ratios of cancer diagnosis by per-interquartile increase in PM_{10} and O_3 exposure using multiple logistic regression analysis after adjusting for age, sex, BMI, smoking status, alcohol consumption, physical activity, education, marital status, income, place of residence, and medical history. We then performed a stratified analysis using obesity, age, sex, smoking, alcohol consumption, and physical activity. We conducted all analyses considering the survey weight using SAS software 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

The demographic, socioeconomic, and health-related behavior characteristics of the study population are summarized in **Table 1**. The mean subject age was 47.8 years, and the study population was 50.1% women. Approximately 70% of the participants had lived at the same residence for >20 years. The associations between air pollution, health-related behaviors, socioeconomic factors and cancer diagnosis are presented in **Table 2**. PM_{10} and O_3 were positively associated with cancer (odds ratio [OR] and 95% confidence interval [CI] for PM_{10}: 1.18, 1.06–1.31; O_3: 1.04, 1.01–1.07). Of the health-related behaviors, obesity, ever smoking, and alcohol consumption were associated with a cancer diagnosis.

We confirmed increased cancer risk among obese subjects aged >50 for exposure to both PM_{10} and O_3 in multiple logistic regression analysis (PM_{10}: 50–60 years, 1.40, 1.01–1.96; ≥ 60 years, 1.34, 1.03–1.74; and O_3: 50–60 year, 1.20, 1.08–1.33; ≥ 60 years, 1.12, 1.04–1.20; **Table 3**.). However, subjects younger than 50 years did not experience an increase in cancer risk even if they were obese. While we observed an increased risk of cancer from PM_{10} exposure for obese men aged 50 and, but not for obese women. Non-obese women aged 50–60 years showed a higher risk of cancer from PM_{10} exposure than obese-women of the same age. For O_3 exposure, all obese subjects aged 50 and older had an increased risk of cancer diagnosis, while non-obese subjects were not at significantly increased risk.

The cancer diagnosis risk for the interquartile exposure to PM_{10} and O_3 according to age, obesity, and health-related behaviors is shown in **Figure 1**. Obese subjects with ≥50 years old who reported unhealthy behaviors had an increased risk of cancer diagnosis. When we stratified by smoking status, obese ever-smokers aged 50–60 who had been exposed to PM_{10} were at greater risk of cancer diagnosis than non-obese ever-smokers of the same age group (**Figure 1A**). For O_3 exposure, obese subjects ≥50 years were at increased risk of cancer regardless of smoking status, and non-obese ever-smokers aged ≥60 years also showed increased cancer risk (**Figure 1B**). We found no trends associated with alcohol consumption, although obese subjects aged ≥50 who reported no alcohol consumption had an increased risk of cancer diagnosis with PM_{10} and O_3 exposure. Obese subjects aged ≥60 who reported regular alcohol consumption and who had PM_{10} exposure and obese subjects aged 50–60 who reported regular alcohol consumption and who had O_3 exposure both faced an increased risk of cancer diagnosis (**Figure 1 C, D**). Non-obese subjects aged 50–60 years who reported regular alcohol consumption were at an increased cancer risk if they also had PM_{10} exposure. However, we found no

association between cancer risk, O_3 exposure, and alcohol consumption status in non-obese subjects (**Figure 1D**). The cancer diagnosis risk for exposure to PM_{10} or O_3 was significantly higher among obese inactive subjects who were ≥50 years old. Despite their obesity, subjects <50 years old who were physically active had a decreased risk of cancer, but this risk was not significant (**Figure 1 E, F**).

Discussion

In this study, long-term exposure to PM_{10} and O_3 was found to increase cancer risk. In particular, the effect of PM_{10} on cancer risk differed according to age, sex, obesity status, and health-related behaviors. Regarding O_3 exposure, cancer risk was strongly influenced by age and obesity. Finally, we found that long-term exposure to PM_{10} and O_3 did not increase cancer risk among subjects who practiced healthy behaviors, compared with subjects who practiced unhealthy behaviors. Although alcohol consumption is a well-established risk factor of cancer, the effect on the cancer risk for PM_{10} and O_3 exposure was not proven.

The incidence of most cancers increases with age, with more rapid increases at the onset of midlife. Obesity and unhealthy behaviors affect to health status significantly in midlife (21). These multifactorial causes may lead to functional declines at the cellular, tissue, and organ levels, which can be augmented by air pollution, significantly elevating cancer risk among people 50 years and older (22). Our findings are compatible with a previous report stating that the age-specific incidence of common cancers rapidly increased after age 50 for both men and women in Korea and old people were susceptible to the exposure of air pollution (23,24). Even more subjects 50–60 years old with unhealthy behaviors exhibited higher cancer risk than subjects aged ≥60 years in stratified analysis in the present study. Exposure-response may help explain uncertainties; subjects 50–60 years old frequently exposed to pollutants with high activity compared with subjects aged ≥60 years (24,25).

Interestingly, the effects of sex and health-related behaviors on the associations between PM_{10} and O_3 exposure and cancer risk were markedly stronger in obese subjects. Obesity-induced pro-inflammatory cytokines, which increase oxidative stress-induced DNA damage, are associated with the development and progression of cancer (26). Poly-aromatic hydrocarbons from air pollutants affect individual antioxidant activity, DNA repair, cell proliferation, and apoptosis (27). Inflammation of gut lining epithelial cells, after ingestion or

inhalation, affect immune response and the gut microbiota in aero-digestive cancer (14). A case–control study of indoor air pollution from solid fuels on esophageal cancer and an ecological study of metallic emissions on liver and colorectal cancers have also indicated similar associations of air pollutants with cancer (28,29). Additionally, epigenetic approaches to analyzing DNA methylation changes have suggested it to be one of the biological mechanisms behind these associations (24).

Obese men ≥ 50 years old with PM_{10} exposure had particularly elevated cancer risk, whereas non-obese women aged 50–60 years with PM_{10} exposure faced relatively increased cancer risk. In the Veterans Affairs Normative Aging Study, obese–men were most susceptible to air pollution's effects on cancer risk, similar to our study (30). These sex differences in the effects of air pollution exposure could be explained by sex-related variation in hormones and body size, which could influence biological transport of pollutants in the body (31). In a rodent model exposed to highly polluted air, brain and epididymal fat mass were significantly elevated in males (32). The obesity-related sex differences observed in the present study offers explanatory insight into increased cancer risk in men. However, a meta-analysis of 19 prospective cohort studies could not identify any sex differences in lung-cancer mortality according to air-pollutant exposure (33). Known cancer risk factors that vary according to sex, such as hypertension and socioeconomic factors, may have influenced other variables. Given the inconsistent findings among several studies, further research is needed to explore risk across different races and cancer types.

Previous studies confirmed that lung cancer mortality and incidence were elevated among smokers with air pollution exposure; meanwhile, other studies reported increased lung cancer mortality and incidence rates among non-smokers or null associations for long-term exposure to ambient fine particles (4,5,34). Smoking enhances oxidative stress not only through the production of reactive oxygen radicals, but also through the weakening of antioxidant defense mechanisms. Therefore, the different cancer risk of subjects according to smoking status likely relates to variation in lung deposition and competition for metabolic activation (35,36).

In this study, physical activity was negatively associated with cancer diagnosis. Regular exercise is thought to increase antioxidant capacity and to have anti-inflammatory effects, leading to a protective effect against cancer (37). Inconsistent finding with alcohol consumption is similar with Strak et al.'s study (13), which the association between air pollutants and alcohol consumption disappeared according to drinking pattern.

In our study, participants were classified as drinkers based on consumption of more than one drink per week; thus, the influence of alcohol on cancer risk might have been underestimated.

This study extended the association of cancer risk on the exposure of PM_{10} and O_3 regarding the significant effects of smoking and physical activity, especially after stratifying by age and obesity to better understand confounding factors in these relationships.

This study has several limitations. First, establishment of causality was impossible because of the cross-sectional design. Second, cancer data relied on a self-reported diagnosis history, which may have biased the findings. Due to the lack of information about the timing and type of cancer diagnoses, we could only estimate the risk for all-cancer diagnosis with long-term exposure to PM_{10} and O_3. Because the PM_{10} and O_3 were measured from 2003 to 2012 in Korean Air Pollutants Emission Service, the findings should not be generalized to the other exposure time considering latency period. Furthermore, we could not obtain measurements of $PM_{2.5}$; therefore, the association between $PM_{2.5}$ and cancer risk could not be evaluated in this study. Third, we matched participants' community of residence and local PM_{10} and O_3 levels using residential territories. Therefore, our matching system would not accurately reflect air-pollutant exposure levels if participants spent a lot of time away from their area of residence. Fourth, we could not obtain data on traffic-related air pollution, which may be a main source of PM in Korea (38). Although PM_{10} plays a role in the formation of O_3 through photochemical processes, we could not assess additive risks of PM_{10} and O_3 from the KCHS data. However, measuring exposure to PM_{10} and O_3 for ≥10 years in 16 Korean metropolitan areas and provinces could overcome the temporal-spatial variation (39). Finally, other important cancer risk factors, such as nutrition and genetics, were not considered in our models.

Conclusions

Long-term exposure to PM_{10} and O_3 is associated with elevated cancer risk, which is compounded by obesity, smoking, and physical inactivity among Koreans aged 50 years and older. Therefore, the cancer risk associated with air pollution exposure could be reduced by individual lifestyle modification, while community-level reductions will likely result from policies decreasing air pollution.

Acknowledgements

The authors would like to thank the Korea Centers for Disease Control and Prevention for Community Health Survey 2012, and the National Institute of Environmental Research, 2003-2012.

References

1. IARC. IARC monographs on the evaluation of carcinogenic risks to humans. International Agency for Research on Cancer2013. 1-454 p.
2. WHO air quality quidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide, Global update 2005. 20 Avenue Appia, 1211 Geneva 27, Switzerland: World Health Organization; 2006.
3. Aaron J. Cohen HRA, Bart Ostro,, Kiran Dev Pandey MK, Nino Künzli KG, C. Arden Pope III IR, Smith JMSaKR. Urban air pollution. Volume Vol. 2, Comparative quantification of health risks: global and regional burden of disease due to selected major risk factors: World Health Organization; 2004. p 1353-434.
4. Hystad P, Demers PA, Johnson KC, Carpiano RM, Brauer M. Long-term residential exposure to air pollution and lung cancer risk. Epidemiology **2013**;24(5):762-72 doi 10.1097/EDE.0b013e3182949ae7.
5. Turner MC, Krewski D, Pope CA, 3rd, Chen Y, Gapstur SM, Thun MJ. Long-term ambient fine particulate matter air pollution and lung cancer in a large cohort of never-smokers. American journal of respiratory and critical care medicine **2011**;184(12):1374-81 doi 10.1164/rccm.201106-1011OC.
6. Liu CC, Tsai SS, Chiu HF, Wu TN, Chen CC, Yang CY. Ambient exposure to criteria air pollutants and risk of death from bladder cancer in Taiwan. Inhal Toxicol **2009**;21(1):48-54 doi 10.1080/08958370802207326.
7. Pan WC, Wu CD, Chen MJ, Huang YT, Chen CJ, Su HJ, *et al.* Fine Particle Pollution, Alanine Transaminase, and Liver Cancer: A Taiwanese Prospective Cohort Study (REVEAL-HBV). J Natl Cancer Inst **2016**;108(3) doi 10.1093/jnci/djv341.
8. Parent ME, Goldberg MS, Crouse DL, Ross NA, Chen H, Valois MF, *et al.* Traffic-related air pollution and prostate cancer risk: a case-control study in Montreal, Canada. Occup Environ Med **2013**;70(7):511-8 doi 10.1136/oemed-2012-101211.
9. Raaschou-Nielsen O, Andersen ZJ, Hvidberg M, Jensen SS, Ketzel M, Sorensen M, *et al.* Air pollution from traffic and cancer incidence: a Danish cohort study. Environ Health **2011**;10:67 doi 10.1186/1476-069X-10-67.

10. Ancona C, Badaloni C, Mataloni F, Bolignano A, Bucci S, Cesaroni G, *et al.* Mortality and morbidity in a population exposed to multiple sources of air pollution: A retrospective cohort study using air dispersion models. Environ Res **2015**;137:467-74 doi 10.1016/j.envres.2014.10.036.

11. Andersen ZJ, Ravnskjaer L, Andersen KK, Loft S, Brandt J, Becker T, *et al.* Long-term Exposure to Fine Particulate Matter and Breast Cancer Incidence in the Danish Nurse Cohort Study. Cancer Epidemiol Biomarkers Prev **2017**;26(3):428-30 doi 10.1158/1055-9965.EPI-16-0578.

12. Reding KW, Young MT, Szpiro AA, Han CJ, DeRoo LA, Weinberg C, *et al.* Breast Cancer Risk in Relation to Ambient Air Pollution Exposure at Residences in the Sister Study Cohort. Cancer Epidemiol Biomarkers Prev **2015**;24(12):1907-9 doi 10.1158/1055-9965.EPI-15-0787.

13. Strak M, Janssen N, Beelen R, Schmitz O, Karssenberg D, Houthuijs D, *et al.* Associations between lifestyle and air pollution exposure: Potential for confounding in large administrative data cohorts. Environ Res **2017**;156:364-73 doi 10.1016/j.envres.2017.03.050.

14. Wong CM, Tsang H, Lai HK, Thomas GN, Lam KB, Chan KP, *et al.* Cancer Mortality Risks from Long-term Exposure to Ambient Fine Particle. Cancer Epidemiol Biomarkers Prev **2016**;25(5):839-45 doi 10.1158/1055-9965.EPI-15-0626.

15. Lakey PS, Berkemeier T, Tong H, Arangio AM, Lucas K, Poschl U, *et al.* Chemical exposure-response relationship between air pollutants and reactive oxygen species in the human respiratory tract. Scientific reports **2016**;6:32916 doi 10.1038/srep32916.

16. Poma A, Colafarina S, Aruffo E, Zarivi O, Bonfigli A, Di Bucchianico S, *et al.* Effects of ozone exposure on human epithelial adenocarcinoma and normal fibroblasts cells. PLoS One **2017**;12(9):e0184519 doi 10.1371/journal.pone.0184519.

17. Hoogervorst EM, de Vries A, Beems RB, van Oostrom CT, Wester PW, Vos JG, *et al.* Combined oral benzo[a]pyrene and inhalatory ozone exposure have no effect on lung tumor development in DNA repair-deficient Xpa mice. Carcinogenesis **2003**;24(3):613-9.

18. Cakmak S, Hebbern C, Pinault L, Lavigne E, Vanos J, Crouse DL, *et al.* Associations between long-term PM2.5 and ozone exposure and mortality in the Canadian Census Health and Environment Cohort (CANCHEC), by spatial synoptic classification zone. Environ Int **2018**;111:200-11 doi 10.1016/j.envint.2017.11.030.

19. Seo J, Choi B, Kim S, Lee H, Oh D. The relationship between multiple chronic diseases and depressive symptoms among middle-aged and elderly populations: results of a 2009 korean community health survey of 156,747 participants. BMC public health **2017**;17(1):844 doi 10.1186/s12889-017-4798-2.

20. Sun Taek Kim. Quality control of Air pollution Monitoring System and establishment of Data Evaluation Scheme(I). Korean Air Pollutants Emission Service2015.

21. Prasad S, Sung B, Aggarwal BB. Age-associated chronic diseases require age-old medicine: role of chronic inflammation. Prev Med **2012**;54 Suppl:S29-37 doi 10.1016/j.ypmed.2011.11.011.

22. Chen H, Goldberg MS, Villeneuve PJ. A systematic review of the relation between long-term exposure to ambient air pollution and chronic diseases. Reviews on environmental health **2008**;23(4):243-97.

23. Jung K-W, Won Y-J, Oh C-M, Kong H-J, Lee DH, Lee KH, *et al.* Cancer Statistics in Korea: Incidence, Mortality, Survival, and Prevalence in 2014. Cancer Research and Treatment : Official Journal of Korean Cancer Association **2017**;49(2):292-305 doi 10.4143/crt.2017.118.

24. Ruckerl R, Schneider A, Breitner S, Cyrys J, Peters A. Health effects of particulate air pollution: A review of epidemiological evidence. Inhal Toxicol **2011**;23(10):555-92 doi 10.3109/08958378.2011.593587.

25. Shin J, Park JY, Choi J. Long-term exposure to ambient air pollutants and mental health status: A nationwide population-based cross-sectional study. PLoS One **2018**;13(4):e0195607 doi 10.1371/journal.pone.0195607.

26. Marseglia L, Manti S, D'Angelo G, Nicotera A, Parisi E, Di Rosa G, *et al.* Oxidative stress in obesity: a critical component in human diseases. Int J Mol Sci **2014**;16(1):378-400 doi 10.3390/ijms16010378.

27. Risom L, Moller P, Loft S. Oxidative stress-induced DNA damage by particulate air pollution. Mutat Res **2005**;592(1-2):119-37 doi 10.1016/j.mrfmmm.2005.06.012.

28. Sapkota A, Zaridze D, Szeszenia-Dabrowska N, Mates D, Fabianova E, Rudnai P, *et al.* Indoor air pollution from solid fuels and risk of upper aerodigestive tract cancers in central and eastern Europe. Environ Res **2013**;120:90-5 doi 10.1016/j.envres.2012.09.008.

29. Garcia-Perez J, Lopez-Cima MF, Perez-Gomez B, Aragones N, Pollan M, Vidal E, *et al.* Mortality due to tumours of the digestive system in towns lying in the vicinity of metal production and processing

installations. The Science of the total environment **2010**;408(16):3102-12 doi 10.1016/j.scitotenv.2010.03.051.

30. Baja ES, Schwartz JD, Wellenius GA, Coull BA, Zanobetti A, Vokonas PS, *et al.* Traffic-related air pollution and QT interval: modification by diabetes, obesity, and oxidative stress gene polymorphisms in the normative aging study. Environmental health perspectives **2010**;118(6):840-6 doi 10.1289/ehp.0901396.
31. Clougherty JE. A growing role for gender analysis in air pollution epidemiology. Cien Saude Colet **2011**;16(4):2221-38.
32. Wei Y, Zhang JJ, Li Z, Gow A, Chung KF, Hu M, *et al.* Chronic exposure to air pollution particles increases the risk of obesity and metabolic syndrome: findings from a natural experiment in Beijing. FASEB journal : official publication of the Federation of American Societies for Experimental Biology **2016**;30(6):2115-22 doi 10.1096/fj.201500142.
33. Cui P, Huang Y, Han J, Song F, Chen K. Ambient particulate matter and lung cancer incidence and mortality: a meta-analysis of prospective studies. Eur J Public Health **2015**;25(2):324-9 doi 10.1093/eurpub/cku145.
34. McDonnell WF, Nishino-Ishikawa N, Petersen FF, Chen LH, Abbey DE. Relationships of mortality with the fine and coarse fractions of long-term ambient PM10 concentrations in nonsmokers. Journal of exposure analysis and environmental epidemiology **2000**;10(5):427-36.
35. Isik B, Ceylan A, Isik R. Oxidative stress in smokers and non-smokers. Inhal Toxicol **2007**;19(9):767-9 doi 10.1080/08958370701401418.
36. Hoek G, Raaschou-Nielsen O. Impact of fine particles in ambient air on lung cancer. Chinese journal of cancer **2014**;33(4):197-203 doi 10.5732/cjc.014.10039.
37. Radak Z, Chung HY, Goto S. Exercise and hormesis: oxidative stress-related adaptation for successful aging. Biogerontology **2005**;6(1):71-5 doi 10.1007/s10522-004-7386-7.
38. Ryou HG, Heo J, Kim SY. Source apportionment of PM10 and PM2.5 air pollution, and possible impacts of study characteristics in South Korea. Environmental pollution (Barking, Essex : 1987) **2018**;240:963-72 doi 10.1016/j.envpol.2018.03.066.

39. Mauderly JL, Burnett RT, Castillejos M, Ozkaynak H, Samet JM, Stieb DM, *et al.* Is the air pollution health research community prepared to support a multipollutant air quality management framework? Inhal Toxicol **2010**;22 Suppl 1:1-19 doi 10.3109/08958371003793846.

Table 1. Baseline characteristics of study population

Variables	Total (n=100,867)	Men (n=50,333)	Women (n=50,534)
Age, years	47.8±0.06	46.6±0.07	49.1±0.07
Obesity (%)	23.4	29.0	17.7
Smoking, n (%)			
Ever	37.0	73.7	5.8
Never	63.0	26.3	94.2
Alcohol consumption, n (%)			
Never/ Less than one time per week	88.3	84.4	92.2
More than one time per week	11.7	15.6	7.8
Physical activity, (%)			
Active	43.7	48.9	36.2
Inactive	56.3	51.1	63.8
Education, years (%)			
< 9	28.0	19.1	35.7
≥ 9	72.0	80.9	64.3
Marital status, (%)			
Married/with partner	65.0	67.4	62.7
Divorced/widowed/unmarried	35.0	32.6	37.3
Household income, won/month (%)			
< 1,000,000	17.7	15.2	20.1
≥ 1,000,000	81.3	84.8	79.9
Residence of urban (%)	79.5	79.5	79.5
Length of residence			
10-15 years	16.3	15.4	17.1
15-20 years	13.6	13.3	13.9

≥ 20 years	70.1	71.3	69.0
Hypertension (%)	20.0	19.4	20.5
Diabetes mellitus (%)	7.6	8.0	7.2
Dyslipidemia (%)	11.1	10.4	11.8
Stroke (%)	1.5	1.6	1.3
Myocardial infarction (%)	1.2	1.5	0.9
Ischemic heart disease (%)	1.5	1.5	1.5
Asthma (%)	2.6	2.3	2.8
Cancer (%)	3.0	2.6	3.5

Data was shown by mean and standard error or percentage. Physical active group was defined as moderate intense activity ≥ 3 times per week or vigorous activity ≥1 time per week. Inactive group was not met these criteria. Length of residence with same domicile was counted. Obesity was defined as more than 25 of body mass index.

Table 2. Univariate analysis of air pollutants, health-related behaviors, socioeconomic factors and cancer diagnosis

Variables	Cancer
PM_{10}	1.18(1.06,1.31)
O_3	1.04(1.01,1.07)
Age	1.05(1.04,1.05)
Sex (men)	1.13(1.04,1.22)
Body mass index (≥ 25)	1.12(1.03, 1.22)
Smoking, Ever	1.21(1.12, 1.30)
Alcohol consumption, more than one time per week	1.73(1.55, 1.93)
Physical activity, inactive	0.97(0.98, 1.04)
Education, < 9 years	0.98(0.89, 1.07)
Marital status, divorced/widowed/unmarried	1.72(1.58, 1.88)
Household income, < 1,000,000 won/month	0.98(0.90, 1.06)
Residence of urban	0.96(0.89, 1.04)
Hypertension	1.09(1.01, 1.18)
Diabetes mellitus	0.83(0.76, 0.92)
Dyslipidemia	0.85(0.77, 0.94)
Stroke	1.07(0.88, 1.30)
Myocardial infarction	0.79(0.63, 1.00)
Ischemic heart disease	1.01(0.83, 1.23)
Asthma	0.93(0.79, 1.10)

Table 3. The risk of cancer diagnosis for the exposure of PM_{10} and O_3 according to obesity, age and sex

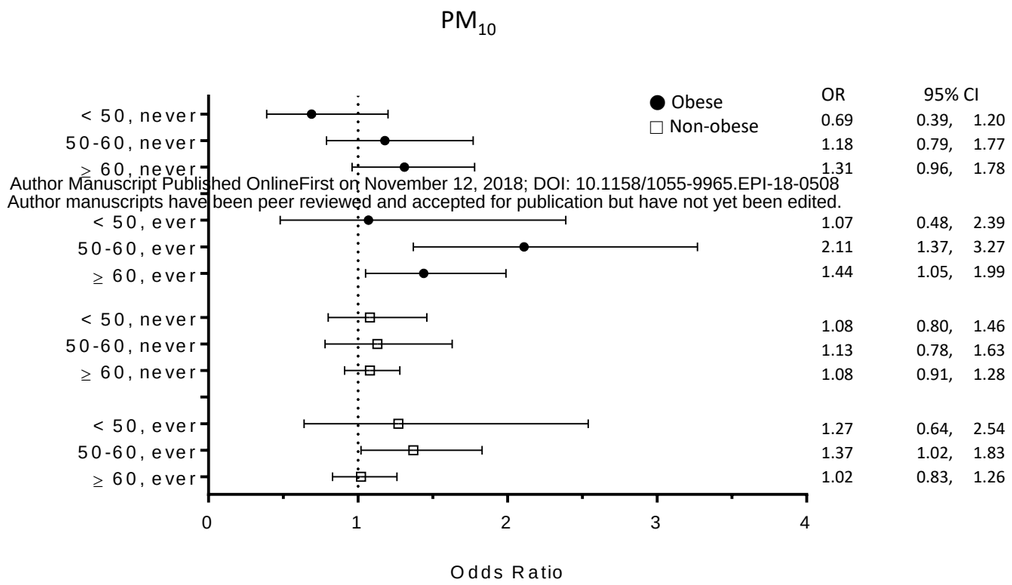
		PM_{10}						O_3					
		Non-obese			Obese			Non-obese			Obese		
Age (year)	Sex	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
60 >=		1.03	0.88,	1.20	1.34	1.03,	1.74	1.01	0.97,	1.05	1.12	1.04,	1.20
50–60		1.25	0.98,	1.60	1.40	1.01,	1.96	1.03	0.96,	1.10	1.20	1.08,	1.33
50 <		1.14	0.86,	1.52	0.74	0.44,	1.23	1.02	0.94,	1.11	0.91	0.79,	1.05
60 >=	Men	1.05	0.86,	1.29	1.50	1.04,	2.04	1.06	0.98,	1.16	1.07	1.01,	1.13
	Women	1.00	0.82,	1.20	1.25	0.94,	1.67	0.95	0.90,	1.01	1.17	1.08,	1.28
50–60	Men	1.11	0.77,	1.60	1.87	1.17,	3.01	1.01	0.91,	1.12	1.27	1.06,	1.51
	Women	1.34	1.00,	1.81	1.17	0.82,	1.68	1.04	0.96,	1.13	1.17	1.07,	1.28
50 <	Men	1.17	0.62,	2.20	1.31	0.99,	1.73	0.97	0.82,	1.15	0.91	0.74,	1.12
	Women	1.03	0.76,	1.40	0.64	0.35,	1.17	1.04	0.95,	1.13	0.92	0.79,	1.06

Multiple logistic regression analysis was performed according to obesity and age after adjusting for sex, smoking, physical activity, alcohol consumption, education, marital status, income, residence, and medical history, except for the selected stratification variable.

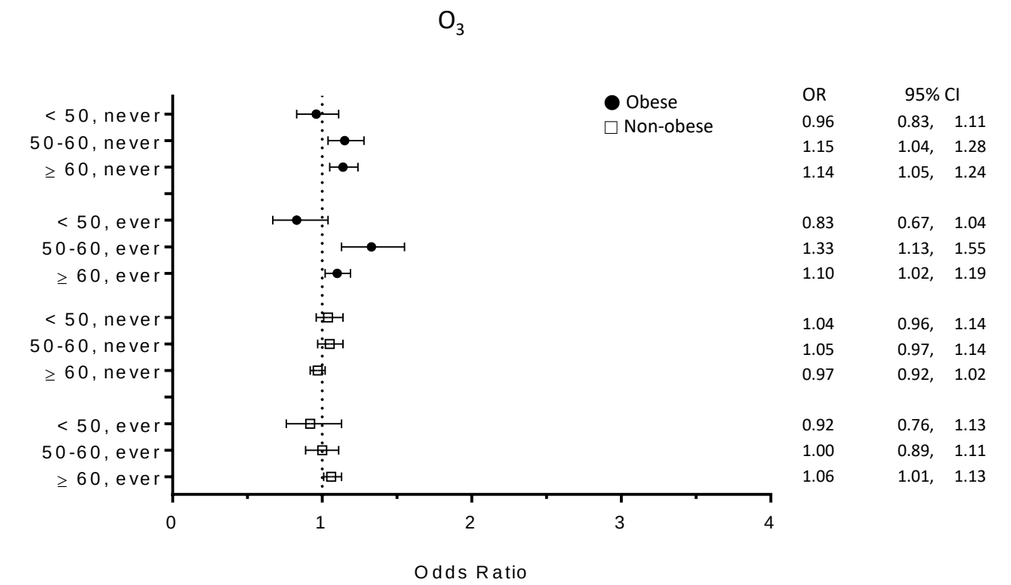
Figure Legend

Figure 1. Cancer risk from exposure to particulate matter and ozone according to health-related behaviors.

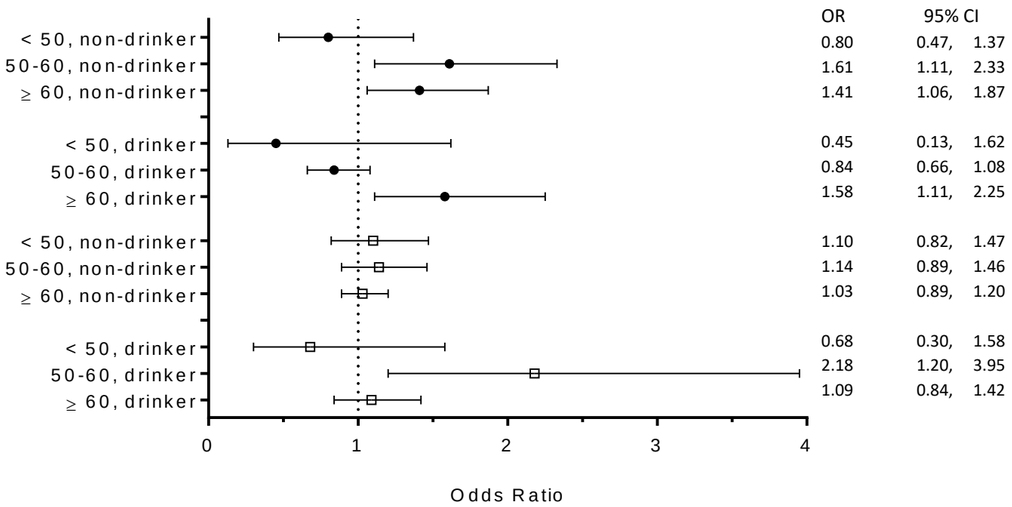
Multiple logistic regression analysis was performed after adjusting for age, sex, smoking, physical activity, alcohol consumption, education, marital status, income, residence, and medical history, except for the selected stratification variable.



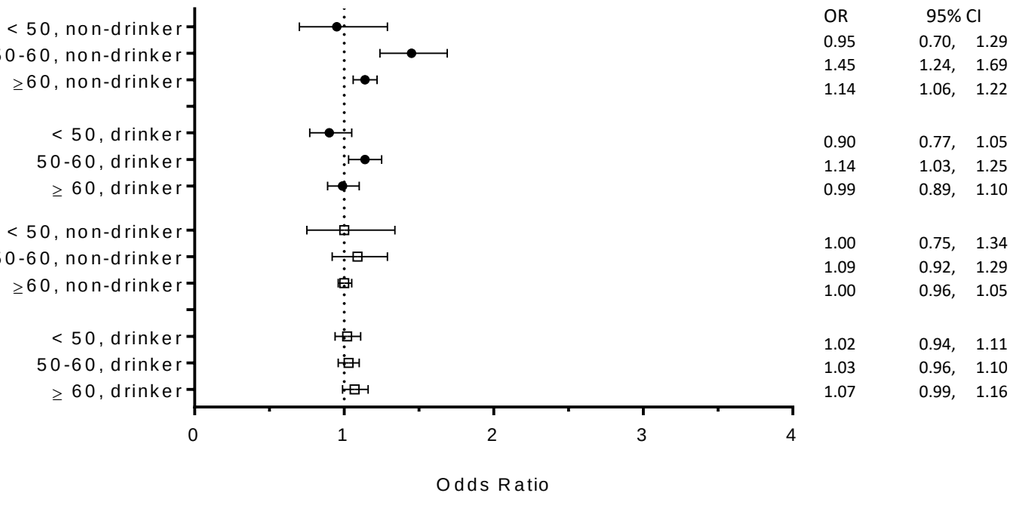
A) Odds of cancer risk according to smoking status (PM_{10})



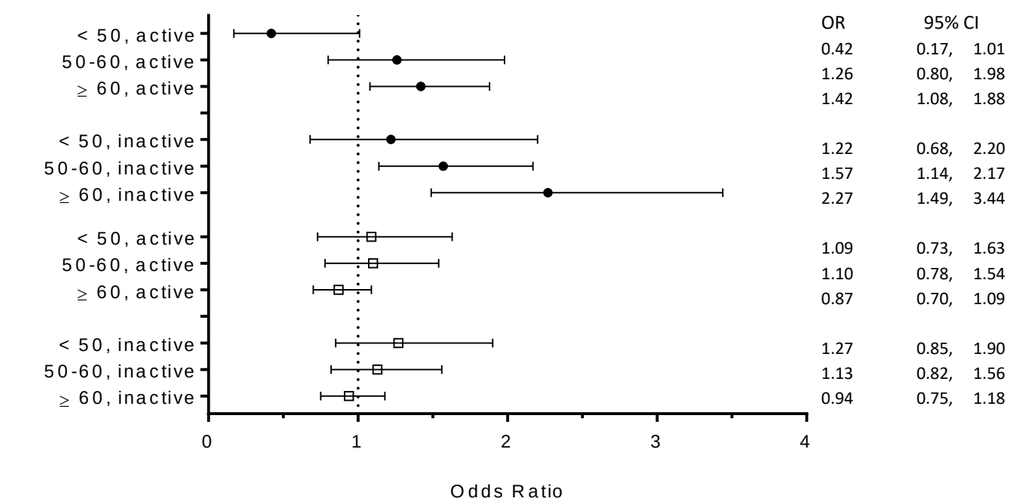
B) Odds of cancer risk according to smoking status (O_3)



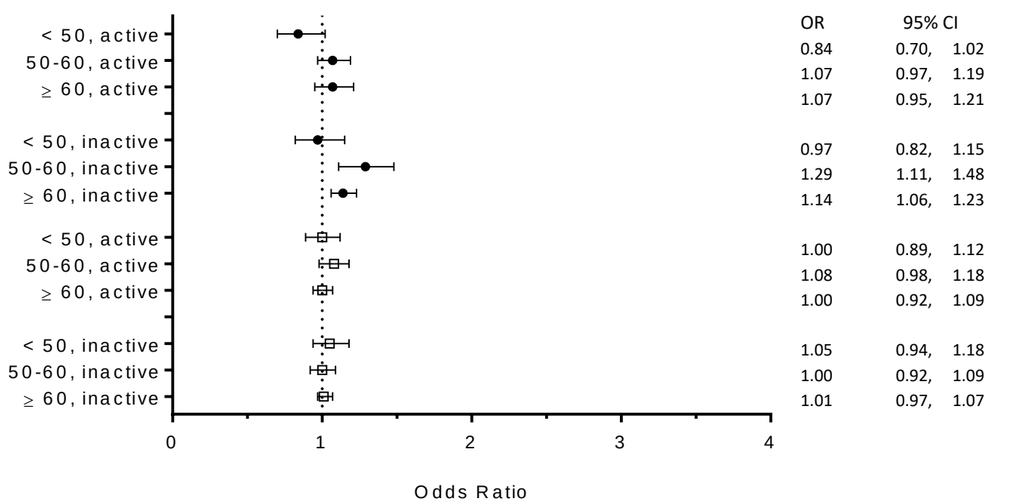
C) Odds of cancer risk according to drinking status (PM_{10})



D) Odds of cancer risk according to drinking status (O_3)



E) Odds of cancer risk according to physical activity (PM_{10})



F) Odds of cancer risk according to physical activity (O_3)

Cancer Epidemiology, Biomarkers & Prevention

AACR American Association for Cancer Research

Cancer risk from exposure to particulate matter and ozone according to obesity and health-related behaviors: A nationwide population-based cross-sectional study

Kyoung Jin Kim, Jinyoung Shin and Jaekyung Choi

Cancer Epidemiol Biomarkers Prev Published OnlineFirst November 12, 2018.