Cancer risk in road transportation workers: a national representative cohort study with 600,000 person-years of follow-up

Wanhyung Lee1, Mo-Yeol Kang2, Ji hyun Kim3,4, Sung-Shil Lim3,4 & Jin-Ha Yoon4,5*

We analysed cancer risk in road transportation workers (RTWs) exposed to traffic air pollution and motor vehicle engine exhaust using the Korean National Health Insurance Service database. RTWs were defined as individuals in the transportation workers group doing road transportation. First admission history of cancer within a 3-year wash-out period was defined as an incident case. The crude incidence, standardised incidence ratio (SIR), and 95% confidence interval (CI) of all cancer risk of RTWs were compared with those of government employees or the whole working population. In total, 3,074 cancer cases were found among RTWs. The respective SIRs and 95% CIs for cancers in RTWs compared with those in the whole population were as follows: liver and intrahepatic bile duct cancers, 1.15 and 1.04–1.27; other digestive organ cancers, 1.28 and 1.04–1.57; trachea, bronchus, and lung cancers, 1.28 and 1.15–1.43; and bladder cancer, 1.26 and 1.03–1.52, respectively. The corresponding SIRs and 95% CIs were also higher in RTWs than in government employees. RTWs have a high risk of developing cancer, including cancer in the liver, intrahepatic bile ducts, other digestive organs, trachea, bronchus, lung, and bladder. Our results can assist in establishing prevention strategies for various cancers in RTWs.

Road transport workers (RTWs) such as truck, bus, and taxi drivers account for approximately 3% of the working-age population in Korea1. RTWs face accident risks and injury by motor vehicles and are exposed to various chemicals, including motor engine exhaust2.

Motor engine exhaust is a complex mixture of particulates and gases2. Various hydrocarbons and derivatives (such as benzene, formaldehyde, toluene, and sulphur dioxide); inorganic sulphates and nitrates; metals, including lead and platinum; and polycyclic aromatic hydrocarbons (PAHs) make up the mixture of particulates and gases from vehicle engine exhaust1. The International Agency for Research on Cancer (IARC) reviewed the literature and categorised diesel engine exhaust (DEE) as a Group 1 carcinogen, indicating ‘carcinogenic to humans’, in 2012. They confirmed its carcinogenicity for lung cancer and reported a positive association with bladder cancer.

The IARC 2012 report showed that engine exhaust increased risk of cancers, such as brain tumours4, colorectal cancer5, and breast cancer6. Furthermore, animal studies and cellular experiments have shown that a significant relationship exists between engine exhaust and various cancer risks other than lung cancer7. One recent cohort study that assessed traffic air pollution exposure for 20 years showed an increased odds of lung, bladder, kidney, and prostate cancer8. Studies have shown when inhaled, fine particles can go through the systemic circulation and consequently cause DNA damage, which is linked to carcinogenesis9–11. However, there is a lack of studies about the association between traffic exhaust and gastrointestinal tract cancers. A well designed pooling analysis of four cohorts showed that the hazard ratio of liver cancer was elevated, but it did not reach statistical significance. Hence, comprehensive studies including all cancer risks related to RTWs are needed. Previous Asian studies...

---

1Department of Occupational and Environmental Medicine, Gil Medical Center, Gachon University College of Medicine, Incheon, Republic of Korea. 2Department of Occupational and Environmental Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea. 3Graduate School of Public Health, Yonsei University, Seoul, Republic of Korea. 4The Institute for Occupational Health, Department of Preventive Medicine, Yonsei University College of Medicine, 50, Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea. 5Department of Preventive Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea. *email: flyinyou@yuhs.ac
with large sample sizes have demonstrated occupational classification-specific cancer risks.

Most well designed exposure assessments are based on a job-exposure matrix (JEM) such as NOCCA-JEMs. JEM is not well-established in non-Western settings, and workers often change their jobs during working periods. Therefore, alternative study designs are needed. Therefore, with current dataset, we aimed to analyze all cancer risks faced by RTWs who are exposed to traffic engine exhaust. We used a national representative cohort study with around 600,000 person-years of RTW data to gain scientific evidence about cancer risks among RTWs. Our subgroup analysis that examines lifestyle differences can give more insight regarding epidemiological evidence. Furthermore, we undertook a sensitivity analysis by accounting for job change over the study period to determine bias of occupational exposure.

### Results

As shown in Table 1, from 2006 to 2015, there were 594,629 person-years for RTWs, 3,268,312 for government employees, and 62,760,615 for the whole working population. The most common age groups were 50–54 among RTWs (20.3%), 55–59 among government employees (19.0%), and 40–44 in the whole working population (18.3%).

Table 2 shows all cases of cancer, the crude incidence of all cancers per 100,000 persons, and the direct age-standardised incidence ratio (SIR) of all cancers and 95% confidence intervals [CIs] among RTWs during the study period. A total of 3,074 cases of cancer were found among RTWs. The annual crude incidence of all cancers per 100,000 persons was as low as 343.66 (2006) and as high as 481.15 (2013). The direct age-SIRs of all cancers were significantly higher in RTWs than in the whole working population in the study period.

Each cancer risk with SIR and 95% CI in the first 1 year fixed exposure cohort is shown in Fig. 1. The cancer incidence was significantly higher in RTWs than in the referenced whole working population for cancers of the liver and intrahepatic bile ducts (SIR 1.15, 95% CI 1.04–1.27), other digestive organs (SIR 1.28, 95% CI 1.19–1.37), and respiratory system (SIR 1.28, 95% CI 1.19–1.37).
1.04–1.57), trachea, bronchus, and lung (SIR 1.28, 95% CI 1.15–1.43), and bladder (SIR 1.26, 95% CI 1.03–1.52). They were also higher when using government employees as a reference.

These significances were not attenuated when using the first 3 years fixed exposure and dynamic cohort definitions (Table 3), except for cancer of the liver and intrahepatic bile ducts referenced from the whole working population (SIR: 1.14, 95% CI 0.99–1.30).

Comparison of the health status using the national health examination between RTWs and the whole working population is found in Supplementary Table 1. Most health measures were statistically similar in RTWs and the whole working population group. When examining HDL-cholesterol level and AST level, the RTW group was healthier than the whole working population, which differed from our expectation (Supplementary Table 1). Only regular exercise levels were significantly lower in RTWs than in the whole working population.

Discussion

Our national representative cohort analysis highlighted that RTWs have a high risk of cancer, including cancer of the liver and intrahepatic bile ducts, other digestive organs, trachea, bronchus, lung, and bladder. Those relationships were not altered after a sensitivity analysis accounting for job exposure change.

Various articles show that professional drivers are exposed to occupational hazards such as shift work, long working hours, biochemicals and toxic materials, social isolation, and lack of decision-making authority.

Figure 1. Standardised incidence ratio with 95% confidence intervals among land transport male workers reference from government employee and whole working population. This figure was drawn by author of WHL.
exhaust as ‘possibly carcinogenic to humans’ (Group 2B)\textsuperscript{22}. A large retrospective study reported that trucking industry workers who had regular exposure to vehicle exhaust from diesel and other types of vehicles on highways, city streets, and loading docks have a 15–40\% increased risk of lung cancer as years of work increased\textsuperscript{23}. When this study was extended with an exposure assessment on the basis of elemental carbon, lung cancer mortality in trucking industry workers was found to be increased in association with cumulative exposure to elemental carbon after adjusting for employment duration\textsuperscript{24}. Other occupational cohort and case–control studies including various occupations involving exposure to diesel engine exhaust, also supported the findings of these cohort studies on truck industry workers\textsuperscript{25}. Furthermore, the risk of lung cancer was positively associated with exposure to nitrogen dioxide, nitrogen oxide, sulphur dioxide, and fine particulate matter. A meta-analysis showed that occupational exposure to air pollution among professional drivers significantly increased the incidence (meta‐odds ratio [OR] 1.27, 95\% CI 1.19–1.36) and mortality (meta‐OR 1.14, 95\% CI 1.04–1.26) of lung cancer\textsuperscript{26}.

An increased risk of bladder cancer among RTWs has also been reported in many case–control studies, although such risks were not definite in cohort studies. A meta-analysis of 3 cohort studies and 27 case–control studies during 1977–2008 indicated an elevated bladder cancer risk among RTWs and railroad workers\textsuperscript{27}. The RTWs had a higher risk for sedentary lifestyle at the workplace due to their working conditions. Previous studies have reported that sedentary lifestyles are closely linked to various cancers, including bladder cancer\textsuperscript{28,29}. Sedentary behaviours might be related to both increased levels of pro-inflammatory factors and decreased levels of anti-inflammatory factors\textsuperscript{30}. Furthermore, physical activity may reduce systemic inflammation by reducing adipose-related inflammatory cytokines\textsuperscript{31}. RTWs were exposed to chronic sedentary working conditions, which might be a risk factor for cancer.

Liver and intrahepatic bile duct malignancies are a leading cause of death worldwide, and hepatocellular carcinoma (HCC) is a representative malignancy among liver cancers\textsuperscript{32}. The most common causes of liver cancer are lifestyle factors such as alcohol drinking (even moderate) and hepatitis B and C viral infections\textsuperscript{33–35}. Chronic inflammation and oxidative stress are major intermediate aetiologies bridging environmental risk factors and carcinogenesis\textsuperscript{36,37}. Hence, antioxidants may lower the liver cancer incidence, and an animal study showed that dietary antioxidants reduced the risk of HCC in a viral hepatitis animal model\textsuperscript{33,35}. A recent review article suggested carcinogenic chemicals as a possible aetiology for liver malignancy, including acrylamide perfluorooctanoic acid, polychlorinated biphenyls, benzo(a)pyrene, perfluorinated chemicals, and vinyl chloride monomers\textsuperscript{38,39}. These chemicals can cause cytotoxicity and DNA damage, which may lead to liver malignancy.

The results of our study show an increased risk of liver cancer among RTWs. Some studies have supported that relationship, indicating an aetiology of liver cancer due to exposure to fine particles, air pollution, and DEE. A case–control study of 314 Chinese HCC patients showed that patients exposed to indoor air pollution had four times higher odds of developing HCC. The OR with 95\% CI was 2.46 (1.47–4.14) after adjustment for hepatitis B viral infection, liver disease, exposure history of pesticide, and other basic demographic characteristics\textsuperscript{37}. A cohort study with more than 15 years of follow-up, including 464 HCC cases in Taiwan, assessed exposure of fine particulate matter (PM2.5) using regional monitoring data and patients’ residential addresses\textsuperscript{38}. The authors reported that PM2.5 exposure was related to incidence of HCC via an indirect effect of elevated serum alanine transaminase and suggested that PM2.5 causes systemic inflammation, which elevates serum alanine transaminase levels and can cause HCC. The main target organ of fine particles, including DEE, is the respiratory tract.

### Table 3.

| Definition of RTWs, SIR (95\% CI) | First 1 year fixed RTWs | First 3 years fixed RTWs | More than 1 year worked as RTWs |
|----------------------------------|-------------------------|-------------------------|-------------------------------|
| Liver and intrahepatic bile ducts neoplasms | 1.23 (1.12–1.36) | 1.24 (1.08–1.42) | 2.41 (2.23–2.59) |
| Other digestive organs neoplasms | 1.46 (1.18–1.78) | 1.58 (1.19–2.06) | 2.63 (2.25–3.06) |
| Trachea, bronchus and lung neoplasms | 1.48 (1.33–1.65) | 1.47 (1.26–1.70) | 2.79 (2.58–3.02) |
| Bladder neoplasms | 1.41 (1.16–1.71) | 1.50 (1.15–1.93) | 2.55 (2.20–2.93) |

Referenced from the government employee:

- Bladder neoplasms 1.26 (1.03–1.52)
- Bladder neoplasms 1.29 (1.01–1.65)
- Bladder neoplasms 1.72 (1.49–1.98)

Consequently, these hazardous factors can result in certain physical (cardiovascular disease, gastrointestinal disorders, musculoskeletal problems, and cancer), psychological (depression, anxiety, and post-traumatic stress disorder), and behavioural (substance abuse) outcomes\textsuperscript{17–20}.

Engine exhaust is particularly thought to cause lung cancer in RTWs\textsuperscript{21}. Working groups convened by the IARC reviewed the scientific literature and classified DEE as ‘carcinogenic to humans’ (Group 1) and gasoline engine exhaust as ‘possibly carcinogenic to humans’ (Group 2B)\textsuperscript{22}. A large retrospective study reported that trucking industry workers who had regular exposure to vehicle exhaust from diesel and other types of vehicles on highways, city streets, and loading docks have a 15–40\% increased risk of lung cancer as years of work increased\textsuperscript{23}. When this study was extended with an exposure assessment on the basis of elemental carbon, lung cancer mortality in trucking industry workers was found to be increased in association with cumulative exposure to elemental carbon after adjusting for employment duration\textsuperscript{24}. Other occupational cohort and case–control studies including various occupations involving exposure to diesel engine exhaust, also supported the findings of these cohort studies on truck industry workers\textsuperscript{25}. Furthermore, the risk of lung cancer was positively associated with exposure to nitrogen dioxide, nitrogen oxide, sulphur dioxide, and fine particulate matter. A meta-analysis showed that occupational exposure to air pollution among professional drivers significantly increased the incidence (meta‐odds ratio [OR] 1.27, 95\% CI 1.19–1.36) and mortality (meta‐OR 1.14, 95\% CI 1.04–1.26) of lung cancer\textsuperscript{26}.

An increased risk of bladder cancer among RTWs has also been reported in many case–control studies, although such risks were not definite in cohort studies. A meta-analysis of 3 cohort studies and 27 case–control studies during 1977–2008 indicated an elevated bladder cancer risk among RTWs and railroad workers\textsuperscript{27}. The RTWs had a higher risk for sedentary lifestyle at the workplace due to their working conditions. Previous studies have reported that sedentary lifestyles are closely linked to various cancers, including bladder cancer\textsuperscript{28,29}. Sedentary behaviours might be related to both increased levels of pro-inflammatory factors and decreased levels of anti-inflammatory factors\textsuperscript{30}. Furthermore, physical activity may reduce systemic inflammation by reducing adipose-related inflammatory cytokines\textsuperscript{31}. RTWs were exposed to chronic sedentary working conditions, which might be a risk factor for cancer.

Liver and intrahepatic bile duct malignancies are a leading cause of death worldwide, and hepatocellular carcinoma (HCC) is a representative malignancy among liver cancers\textsuperscript{32}. The most common causes of liver cancer are lifestyle factors such as alcohol drinking (even moderate) and hepatitis B and C viral infections\textsuperscript{33–35}. Chronic inflammation and oxidative stress are major intermediate aetiologies bridging environmental risk factors and carcinogenesis\textsuperscript{36,37}. Hence, antioxidants may lower the liver cancer incidence, and an animal study showed that dietary antioxidants reduced the risk of HCC in a viral hepatitis animal model\textsuperscript{33,35}. A recent review article suggested carcinogenic chemicals as a possible aetiology for liver malignancy, including acrylamide perfluorooctanoic acid, polychlorinated biphenyls, benzo(a)pyrene, perfluorinated chemicals, and vinyl chloride monomers\textsuperscript{38,39}. These chemicals can cause cytotoxicity and DNA damage, which may lead to liver malignancy.

The results of our study show an increased risk of liver cancer among RTWs. Some studies have supported that relationship, indicating an aetiology of liver cancer due to exposure to fine particles, air pollution, and DEE. A case–control study of 314 Chinese HCC patients showed that patients exposed to indoor air pollution had four times higher odds of developing HCC. The OR with 95\% CI was 2.46 (1.47–4.14) after adjustment for hepatitis B viral infection, liver disease, exposure history of pesticide, and other basic demographic characteristics\textsuperscript{37}. A cohort study with more than 15 years of follow-up, including 464 HCC cases in Taiwan, assessed exposure of fine particulate matter (PM2.5) using regional monitoring data and patients’ residential addresses\textsuperscript{38}. The authors reported that PM2.5 exposure was related to incidence of HCC via an indirect effect of elevated serum alanine transaminase and suggested that PM2.5 causes systemic inflammation, which elevates serum alanine transaminase levels and can cause HCC. The main target organ of fine particles, including DEE, is the respiratory tract.
but inhaled fine particles can translocate and enter the systemic circulation. Exposure to DEE via oral consumption increased DNA adducts, DNA damage, and apoptosis in liver cells in an animal study. A molecular epidemiological case–control study collected liver tissue from HCC patients and analysed DNA adduction by PAHs, which are a component of DEE and well-known carcinogens on the lung and bladder. The OR (95% CI) of HCC was 3.9 (1.0–14.9) in the third tertile for DNA-PAH adduction after adjusting for age, sex, and HBsAg. Interestingly, the odds of HCC were elevated 20 times by DNA-PAH adduction in HBsAg-positive patients.

Systemic circulation and DNA adduction of fine particles and DEE can explain the increased risk of liver cancer in RTWs in the present study.

Our large sample size study showed a relationship between exposure in RTWs and various cancer risks. However, it had several limitations. The lack of quantitative exposure assessment is our main limitation. Various occupational hazardous factors such as chemicals, dust, and sedentary duration at work can be potential risks or mediating factors for cancer, and RTWs are generally exposed to these hazardous factors. Furthermore, well-structured job-exposure matrices for specific work have not been established for RTWs in Korea. The dose–response relationship could not be analysed in this study due to a lack of information regarding the exact exposure levels of various occupational hazardous factors. Further studies with a more comprehensive exposure assessment are needed. Furthermore, we did not employ a job-exposure matrix such as the NOCCA-JEMs, which is the most fundamental method for exposure assessment. In addition, lifetime and cumulative exposure were not included in this study. Although all three scenario approaches of cohort definition show almost same statistical results, more comprehensive and quantitative exposure assessments are needed to clarify the association between RTWs and the risk of various cancer. Additionally, cancer incidents are defined when there are hospital admission histories. Hence, if patients with cancer visit only outpatient clinics or die without admission, they would not be recorded and there would be an underestimation of incident cases. Those underestimations have no direction with regards to the exposed group or the non-exposed group; hence, non-differential misclassification may have occurred. Consequently, the risk of cancers might instead be a forward to null relationship.

In conclusion, RTWs have a high risk of cancer, including cancer of the liver and intrahepatic bile ducts, other digestive organs, trachea, bronchus, lung, and bladder. Particularly, our results suggested that the IARC classification may have occurred. Consequently, the risk of cancers might instead be a forward to null relationship.

Methods

Ethical consideration. Data of this study were anonymised prior to release to the authors from the National Health Insurance Service (NHIS). The Institute Review Board (IRB) of the Yonsei University Health System, Seoul, Korea, approved this study design (IRB number: Y-2017-0100). This data is secondary data from the Korean NHIS database; therefore, informed consents was not needed.

Data collection. We used data from the Korean NHIS database from 2002 to 2015. The NHIS provides mandatory public health insurance and offers coverage of medical care services, including national health insurance, medical aid, and long-term care insurance, to all Korean citizens. The entire population residing within the territory of Korea is covered by the National Health Insurance of Korea, and all citizens of Korea are expected to join the National Health Security System.

All hospital facility visiting information from the Korean NHIS database were categorised under the standardised protocol of the Korea Classification of Diseases and Causes of Death 4th edition, which corresponds to the International Classification of Diseases, 10th revision (ICD-10). All diagnoses were described based on the ICD-10 codes. The NHIS database included qualification and claims medical service data. The qualification data in the NHIS database included age, sex, region, income, type of insurance, identification number, and family information. Medical service data had records of all covered inpatient and outpatient visits, procedures, and prescriptions. The NHIS provides, free of charge, annual or biennial health screening examinations that include the assessment of chronic disorders, mental health, and lifestyle. We used this health screening examination data to compare lifestyle differences between RTWs and the general population.

Study participants. The NHIS database included 50,908,646 patients in 2011, 51,169,141 in 2012, 51,448,491 in 2013, 51,757,146 in 2014, and 52,034,424 in 2015, which covers approximately 98% of the people living in the territory of Korea. There are two main services in the NHIS in Korea, 97% makes up the medical care sector and 3% of medical aid sector. Medical care includes four types of insurances: employee subscriber, employee dependent, district subscriber, and district dependent. To select the RTWs, first we selected male participants aged between 25 and 69 years with NHIS eligibility as employee subscribers in 2006. Subsequently, we excluded participants who had claims for any cancer from 1 January 2002 to 31 December 2005 to ensure first admission history as the incident case. To select the RTW group, we first defined the transportation working group as those working in section H ‘transportation and storage’ from the most recent Korean national standardised industrial classification, which was developed by the Korea National Statistical Office following the 4th revision of the International Standard Industrial Classification of All Economic Activities in 2008. This section includes the provision of passenger or freight transport by rail, pipeline, road, water, or air and associated activities. RTWs were defined as only those among the workers involved in road transportation. This group includes all land-based transport workers such as bus drivers, taxi drivers, shuttle drivers, others who drive rented private cars, and all freight transport operators on the road. Then we defined the RTWs using three deferent definitions based on job duration during follow-up periods due to job changing, detailed information was in ‘Definition of job exposure’ section. To demonstrate the risk of cancers in RTWs compared with other popu-
Cancers. The NHIS claims for inpatient and outpatient visits, procedures, and prescriptions were coded using the ICD-10, which was adopted in Korea in 1995, and renamed as the Korean Drug and Anatomical Therapeutic Chemical Codes (K-DAC). Cancers were defined those with claims information indicating C00–C97 malignant neoplasms of the eye and adnexa (C69), which were not present in any participants. We excluded female genital organ cancers (C51–58) and other lymphoid, haematopoietic, and related tissue (C88–C90, C96), and other, ill-defined, secondaries, unspecified, and multiple sites (C73–C80, C97). We excluded male genital organs (C17, C23, C24, C26), larynx (C32), trachea, bronchus, and lung (C33, C34), other respiratory and intrathoracic organs (C30, C31, C37–C39), bone and articular cartilage (C40, C41), other digestive organs (C17, C23, C24, C26), larynx (C32), trachea, bronchus, and lung (C33, C34), other respiratory and intrathoracic organs (C30, C31, C37–C39), bone and articular cartilage (C40, C41), malignant melanoma of the skin (C43), other skin (C44), mesothelial and soft tissue (C45–C49), breast (C50), prostate (C61), other male genital organs (C60, C62, C63), bladder (C67), other urinary tract (C64–C66, C68), brain (C71), other parts of the central nervous system (C70, 72), Hodgkin diseases (C81), non-Hodgkin lymphoma (C82–C86), leukaemia (C91–C95), other lymphoid, haematopoietic, and related tissue (C88–C90, C96), and other, ill-defined, secondary, unspecified, and multiple sites (C73–C80, C97). We excluded female genital organ cancers (C51–58) and malignant neoplasms of the eye and adnexa (C69), which were not present in any participants.

Health status. To consider health status by occupation, we used the oldest national health screening examination data that could demonstrate the health status of workers before cancer diagnosis during the study period. A total of 549,222 workers and 5,380 RTWs participated in national health screening examinations. These data included information regarding health behaviour (smoking, alcohol drinking, and exercise level) and anthropometric data (body mass index (BMI)), fasting glucose level, lipid profile, liver function, and blood pressure (hypertension).

Statistical analysis. The crude incidence, SIR, and 95% CI of all cancer risks among the RTW were compared to those of the whole working population after adjusting for age (5-year range) using a direct standardised method by the following year. To calculate direct standardisation, the age-specific cancer incidence was calculated for each 5-year age group among the RTW. These values were then multiplied by age-specific cancer incidence rates and the number of person-years in each age group of the whole working population (the reference group), which made the age-specific expected incidence case. The addition of all age-specific expected cases indicated the total incidence. The ratio of the observed and expected numbers of cases was the direct age-SIR. The whole working population and government employees were used as reference groups, separately for each analysis. If the SIR was more than 1 and the lower limit of the 95% CI was also more than 1, the cancer risk was considered significantly higher in the RTW group than in the reference groups. A mid-P test was used for calculating 95% CIs. For the sensitive analysis, we used three different definitions of the cohort to estimate SIRs and 95% CIs for cancer risk with statistical significance above analysis.

To demonstrate effects of confounding variables, we compared BMI, fasting glucose level, lipid profile, liver function, hypertension, smoking, alcohol drinking, and exercise between RTWs and the whole working population using Student's t-test or chi-squared test. All analyses were conducted using SAS, version 9.4 (SAS Institute, Cary, NC, USA).

Ethical consideration. Data of this study were anonymised prior to release to the authors from the NHIS. The Institute Review Board (IRB) of the Yonsei University Health System, Korea approved this study design (IRB number: Y-2017-0100). This data is secondary data from NHIS, hence informed consent was not needed in current study.

Data availability Data cannot be available in public.
References

1. KOSIS. Industrial statistics in Korean 2015 census data, https://kostat.go.kr/portal/eng/surveyOutline/5/1/index.static (2019).
2. Groves, J. & Cain, J. R. A survey of exposure to diesel engine exhaust emissions in the workplace. Ann. Occup. Hyg. 44, 435–447 (2000).
3. IARC. Diesel and gasoline engine exhausts and some nitroarenes. IARC monographs on the evaluation of carcinogenic risks to humans. 105, 9 (2014).
4. Peters, S. et al. Parental occupational exposure to engine exhausts and childhood brain tumors. Int. J. Cancer 132, 2975–2979. https://doi.org/10.1002/ijc.27972 (2013).
5. Kachuri, L. et al. Workplace exposure to engine exhausts and gasoline engine exhausts and the risk of colorectal cancer in Canadian men. Environ. Health 15, 4. https://doi.org/10.1186/s12940-016-0088-1 (2016).
6. Rai, R., Glass, D. C., Heyworth, J. S., Saunders, C. & Fritschi, L. Occupational exposures to engine exhausts and other PAHs and breast cancer risk: a population-based case-control study. Am. J. Ind. Med. 59, 437–444. https://doi.org/10.1002/ajim.22592 (2016).
7. Steiner, S., Bisig, C., Petri-Fink, A. & Rotten-Rutishauser, B. Diesel fumes: knowledge of adverse effects and underlying cellular mechanisms. Arch. Toxicol. 90, 1541–1553. https://doi.org/10.1007/s00204-016-17365 (2016).
8. Cohen, G. et al. Long-term exposure to traffic-related air pollution and cancer among survivors of myocardial infarction: a 20-year follow-up study. Eur. J. Prev. Cardiol. 24, 92–102. https://doi.org/10.1177/2047487316694151 (2017).
9. Gerlofs-Nijland, M. E. et al. Effect of prolonged exposure to diesel engine exhaust on proinflammatory markers in different regions of the rat brain. Part. Fibre Toxicol. 7, 12. https://doi.org/10.1186/1743-8977-7-12 (2010).
10. Nemmar, A. et al. Passage of intratracheally instilled ultrafine particles from the lung into the systemic circulation in hamster. Am. J. Respir. Crit. Care Med. 164, 1665–1668. https://doi.org/10.1164/ajrccm.164.9.20101036 (2001).
11. Dybdahl, M. et al. DNA adduct formation and oxidative stress in colon and liver of Big Blue rats after dietary exposure to diesel particles. Carcinogenesis 24, 1759–1766. https://doi.org/10.1093/carcin/bgg147 (2003).
12. Pedersen, M. et al. Ambient air pollution and primary liver cancer incidence in four European cohorts within the ESCAPE project. Environ. Res. 154, 226–233. https://doi.org/10.1016/j.envres.2017.01.006 (2017).
13. Lee, H.-E., Zaitsu, M., Kim, E.-A. & Kawachi, I. Cancer incidence by occupation in Korea: longitudinal analysis of a nationwide cohort. Saf. Health at Work 11(1), 41–49. https://doi.org/10.1016/j.shaw.2019.12.004 (2020).
14. Eguchi, H., Wada, K., Prieto-Merino, D. & Smith, D. R. Lung, gastric and colorectal cancer mortality by occupation and industry among working-aged men in Japan. Sci. Rep. 7, 1–7 (2017).
15. Kauppinen, T. et al. Construction of job-exposure matrices for the Nordic Occupational Cancer Study (NOCCA). Acta Oncol. 48, 791–800. https://doi.org/10.1080/02841079092718747 (2009).
16. John, L., Flin, R. & Mears, K. Bus driver well-being review: 50 years of research. Transp. Res. Part F Traffic Psychol. Behav. 9, 49–114 (2006).
17. Yook, J.-H., Lee, D.-W., Kim, M.-S. & Hong, Y.-C. Cardiovascular disease risk differences between bus company employees and non-employees in a Korean city. Transp. Res. Part F Traffic Psychol. Behav. 11, 205–211 (2008).
18. Combs, B., Heaton, K., Raju, D., Vance, D. E., & Sieber, W. K. A descriptive study of musculoskeletal injuries in long-haul truck drivers: a NIOSH national survey. Occup. Environ. Med. 66, 799–800 (2016).
19. Shin, S. Y. et al. Lung cancer and vehicle exhaust in trucking industry workers. Acta Oncol. 55, 115–118 (1998).
20. ARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Diesel and gasoline engine exhausts and some nitroarenes. IARC monographs on the evaluation of carcinogenic risks to humans. 105, 9 (2014).
21. Garshick, E. et al. Lung cancer and vehicle exhaust in trucking industry workers. Environ. Health Perspect. 116, 1327–1332 (2008).
22. Garshick, E. et al. Lung cancer and elemental carbon exposure in trucking industry workers. Environ. Health Perspect. 120, 1301–1306 (2012).
23. Moehner, M. & Wendt, A. J. A critical review of the relationship between occupational exposure to diesel emissions and lung cancer risk. Crit. Rev. Toxicol. 47, 185–224 (2017).
24. Chen, C., Wan, X., Yang, G. & Zou, X. J. Traffic-related air pollution and lung cancer: a meta-analysis. Thoracic Cancer 6, 307–318 (2015).
25. Manju, L., George, P. S. & Mathew, A. Urinary bladder cancer risk among motor vehicle drivers: a meta-analysis of the evidence. Asian Pac. J. Cancer Prev. 1977–2008(10), 287–294 (2009).
26. McTernan, A. Mechanisms linking physical activity with cancer. Nat. Rev. Cancer 8, 205–211 (2008).
27. Keimling, M., Behrens, G., Schmid, D., Jochem, C. & Leitmann, M. The association between physical activity and bladder cancer: a systematic review and meta-analysis. Br. J. Cancer 110, 1862–1870 (2014).
28. Allison, M. A., Jensky, N. E., Marshall, S. J., Bertoni, A. G. & Cushman, M. Sedentary behavior and adiposity-associated inflammation: the multi-ethnic study of atherosclerosis. Am. J. Prev. Med. 42, 8–13 (2012).
29. Vella, C. A. et al. Physical activity and adiposity-related inflammation: the MESA. Med. Sci. Sports Exerc. 49, 915 (2017).
30. Balogh, J. et al. Hepatocellular carcinoma: a review. J. Hepatocell. Carcinoma 3, 41–53. https://doi.org/10.2147/JHC.S61146 (2016).
31. Ghouri, Y. A., Mian, I. & Rowe, J. H. Review of hepatocellular carcinoma: epidemiology, etiology, and carcinogenesis. J. Carcinog. 16, 1. https://doi.org/10.4103/jcar.JCar_9_16 (2017).
32. Zaitsu, M., Takeuchi, T., Kobayashi, Y. & Kawachi, I. Light to moderate amount of lifetime alcohol consumption and risk of cancer in Japan. Cancer 126, 1031–1040 (2020).
33. Yu, M. C. & Yuan, J. M. Environmental factors and risk for hepatocellular carcinoma. Gastroenterology 127, S72–S78 (2004).
34. Erzkoglugil, P., Oral, D., Chao, M. W. & Kocer-Gumusel, B. Hepatocellular carcinoma and possible chemical and biological causes: a review. J. Environ. Pathol. Toxicol. Oncol. 36, 171–190. https://doi.org/10.1615/EnvironPatholToxicolOncol.201702927 (2017).
35. Niu, J., Lin, Y., Guo, Z., Niu, M. & Su, C. The epidemiological investigation on the risk factors of hepatocellular carcinoma: a case-control study in southeast China. Medicine (Baltimore) 95, 2758. https://doi.org/10.1097/MD.00000000000002758 (2016).
36. Pan, W. C. et al. Fine particle pollution, alamine transaminase, and liver cancer: a Taiwanese prospective cohort study (REVEAL-HBV). J. Natl. Cancer Inst. https://doi.org/10.1093/jnci/djx341 (2016).
37. Nemmar, A., Hoylearts, M. E., Hoet, P. H. & Nemery, B. Possible mechanisms of the cardiovascular effects of inhaled particles: systemic translocation and prothrombotic effects. Toxicol. Lett. 149, 243–253. https://doi.org/10.1016/j.toxlet.2003.12.061 (2004).
38. Chen, S. Y. et al. Polycyclic aromatic hydrocarbon-DNA adducts in liver tissues of hepatocellular carcinoma patients and controls. Int. J. Cancer 99, 14–21 (2002).
39. Kauppinen, T. et al. Construction of job-exposure matrices for the Nordic Occupational Cancer Study (NOCCA). Acta Oncol. 48, 791–800 (2009).
40. Cheol Seong, S. et al. Data resource profile: the national health information database of the National Health Insurance Service in South Korea. Int. J. Epidemiol. 46, 799–800 (2016).
43. Gauld, R. et al. Advanced Asia’s health systems in comparison. *Health Policy (Amsterdam, Netherlands)* **79**, 325–336. https://doi.org/10.1016/j.healthpol.2006.01.009 (2006).

44. Kwon, S. Thirty years of national health insurance in South Korea: lessons for achieving universal health care coverage. *Health Policy Plan.* **24**, 63–71. https://doi.org/10.1093/heapol/czn037 (2009).

45. Shin, D. W., Cho, B. & Guallar, E. Korean National Health Insurance database. *JAMA Intern. Med.* **176**, 138–138 (2016).

46. Chou, S. B., Lee, W., Yoon, J.-H., Won, J.-U. & Kim, D. W. Ten-year prediction of suicide death using Cox regression and machine learning in a nationwide retrospective cohort study in South Korea. *J. Affect. Disord.* **231**, 8–14 (2018).

47. Division, U. N. S. *International Standard Industrial Classification of All Economic Activities (ISIC).* (United Nations Publications, 2008).

48. Zaitsu, M. et al. Occupational class and risk of cardiovascular disease incidence in Japan: nationwide, multicenter, hospital-based case-control study. *J. Am. Heart Assoc.* **8**, e01350 (2019).

49. Zaitsu, M. et al. Occupational inequalities in female cancer incidence in Japan: Hospital-based matched case-control study with occupational class. *SSM Popul. Health* **5**, 129–137 (2018).

50. Chun, C., Kim, S., Lee, J. & Lee, S. Republic of Korea. Health system review. *Health Syst. Transit.* **11**, 1–184 (2009).

52. Organization, W. H. *International Statistical Classification of Diseases and Related Health Problems.* Vol. 1 (World Health Organization, 2004).

53. Lim, S.-S. et al. The cumulative incidence and trends of rare diseases in South Korea: a nationwide study of the administrative data from the National Health Insurance Service database from 2011–2015. *Orphanet J. Rare Dis.* **14**, 49 (2019).

**Acknowledgements**

We acknowledge the government authorities of the Department of Big Data Steering, National Health Insurance Service. We thank all the scientists working in the National Health Insurance Service who collected and handled the information from medical claims data of the National Health Insurance. This work was supported by the Korea Health Industry Development Institute through “Social and Environmental Risk Research” funded by Ministry of Health & Welfare (HI19C0052). JH Yoon was awarded that grant. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Author contributions**

W.L. and J.H.Y. conceptualised and designed the study. J.K. and S.S.L. performed the formal analysis. M.Y.K., S.S.L., and J.K. wrote the original draft of the manuscript. J.H.Y. devised and supervised the entire process. W.L. drew Fig. 1 and validated the study. All of the authors read and approved the final manuscript. Figure 1 was drawn by W.L., hence no copyright issues exist for this figure.

**Competing interests**

The authors declare no competing interests.

**Additional information**

Supplementary information is available for this paper at https://doi.org/10.1038/s41598-020-68242-5.

Correspondence and requests for materials should be addressed to J.-H.Y.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher’s note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit http://creativecommons.org/licenses/by/4.0/.

© The Author(s) 2020