BMJ Open

# The association between secondhand smoke exposure and blood lead and cadmium concentration in community dwelling women: The fifth Korea National Health and Nutrition Examination Survey (2010-2012)



| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID: | bmjopen-2015-008218 |
| Article Type: | Research |
| Date Submitted by the Author: | 18-Mar-2015 |
| Complete List of Authors: | Jung, Se Young; Seoul National University Bundang Hospital, Seoul National University College of Medicine, Department of Family Medicine<br>Kim, Suyeon; Seoul National University Hospital, Department of Family Medicine<br>Lee, Kiheon ; Seoul National University Bundang Hospital, Seoul National University College of Medicine, Department of Family Medicine<br>Kim, Joo Young; Seoul National University Bundang Hospital, Seoul National University College of Medicine, Department of Family Medicine<br>Bae, Woo Kyung; Seoul National University Bundang Hospital, Health Promotion Center<br>Lee, Keehyuck; Seoul National University Bundang Hospital, Seoul National University College of Medicine, Department of Family Medicine<br>Han, Jong-Soo; Seoul National University Bundang Hospital, Health Promotion Center<br>Kim, Sarah; Seoul National University Bundang Hospital, Seoul National University College of Medicine, Department of Family Medicine |
| Primary Subject Heading: | Smoking and tobacco |
| Secondary Subject Heading: | Addiction, Health policy, Occupational and environmental medicine, Public health, General practice / Family practice |
| Keywords: | TOXICOLOGY, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, OCCUPATIONAL & INDUSTRIAL MEDICINE, PRIMARY CARE |
| | |

# The association between secondhand smoke exposure and blood lead and cadmium concentration in community dwelling women: The fifth Korea National Health and Nutrition Examination Survey (2010-2012)

**Authors:** Se Young Jung[1], Suyeon Kim[2], Kiheon Lee[3*], Joo Young Kim[4], Woo Kyung Bae[5], Keehyuck Lee[6], Jong-Soo Han[7], Sarah Kim[8]

**Affiliation(s) of authors**

**1,3,4,6,8** Department of Family Medicine, Seoul National University College of Medicine and Seoul National University Bundang Hospital, Seongnam, Korea

**2** Department of Family Medicine, Seoul National University Hospital, Seoul, Korea,

**5, 7** Health Promotion Center, Seoul National University Bundang Hospital**,** Seongnam, Korea

**S. Y. Jung and S. Kim contributed equally to this work as first authors.**

**The e-mail address, telephone and fax numbers of the corresponding author**

82, Gumi-ro, 173 beon-gil, Bundang-gu, Seongnam-si, Gyeongi-do, Korea, Postal code: 463-707

Telephone: 82-31-787-7809, Fax: 82-31-787-4014, E-mail: keyhoney@gmail.com,

**Word count: 3,025**

**Key words:** Secondhand smoke, Lead, Cadmium, Metals, Workplace

## ABSTRACT

**Objectives:** To assess the association between secondhand smoke exposure and blood lead and cadmium concentration in women in S. Korea.

**Design:** Population-based cross-sectional study

**Setting:** South Korea (Korea National Health and Nutrition Examination Survey V)

**Participants:** 1,490 non-smoking women who took part in the fifth Korea National Health and Nutrition Examination Survey (2010-2012), in which blood levels of lead and cadmium were measured.

**Primary outcome measures:** The primary outcome were blood levels of lead and cadmium in accordance to the time of secondhand smoke exposure.

**Results:** The adjusted mean level of blood cadmium in women who were never exposed to secondhand smoking per day was 1.21(0.02)ug/L. Among women who were exposed less than 1 hour per day, the mean cadmium level was 1.13(0.03)ug/L, and for those exposed for more than 1 hour, the mean level was 1.46(0.06)ug/L. In particular, there was a significant association between duration of secondhand smoking and blood cadmium concentration at workplace. The adjusted means of blood cadmium concentration in women who never exposed group, less than 1 hour exposed groups and more than 1 hour exposed group at workplace were 1.20ug/L, 1.24ug/L, 1.50ug/L, respectively

**Conclusions:** This study showed that exposure to secondhand smoke and blood cadmium levels

are associated. Especially, there was a significant association at workplace. Therefore, social and political efforts for reducing the exposure to secondhand smoke at workplace are needed in order to promote a healthier working environment for women

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first study to show that women have elevated blood cadmium levels with increased exposure level to SHS, and there is a correlation between blood cadmium levels and the exposure level to SHS at work.

- We evaluated a nationally representative sample so that the results of our study reflect characteristics of general non-smoking female population in S. Korea.

- We compared the exposure between home and workplace, which have not been evaluated concurrently in previous studies.

- Out study has several weaknesses: First, people who work in areas with higher chance of exposure to lead and cadmium were not considered. However the number of women who work in such areas is very low in S. Korea that it is unlikely to have an effect on the research. Second, the survey was not conducted on metals intake through the consumption of food. However, daily consumption of cadmium and lead through food is low in S. Korea

## INTRODUCTION

Exposures to secondhand smoking (SHS) has been a particular public health concern as it is causally linked to lung cancer, stroke, coronary heart disease, nasal irritation and reproductive

harmful effects in women. [1] There has been significant progress to reduce SHS exposure. However, nearly half (46.4%) of nonsmokers in the United States remain exposed. [1] In S. Korea, 4.9% of men and 16.7% of women were exposed to SHS at home and 55.2% of men and 37.2% of women were exposed to SHS at workplaces in 2011. [2] [3] Overall, more than 30% of non-smoking adults and adolescents are still exposed to secondhand smoke in 2014. [4] Smoke-free policies have shown incremental progress since 1995, but smoking is still permitted in many indoor public places. [4]

Cigarette smoke consists of mainstream smoke from the mouth ends of cigarettes during puffing and sidestream smoke from the lit ends of the cigarettes between puffs. The sidestream smoke can reach deeper areas in the lung because the size and concentration of the particle are smaller and higher, respectively, than that of mainstream smoke. SHS is a mixture of the sidestream smoke and exhaled mainstream smoke [5] and contains more than 4000 chemical compounds known to cause diseases, including nitrosamines, polycyclic aromatic hydrocarbons (PAHs), cadmium, chromium, lead and nickel [5] [6] Lead and cadmium have been particular concerns due to their carcinogenicity, tendency to accumulate in the body and their potential toxicity to the developing fetus [7] [8]

There are strong associations between the blood lead levels and active smoking, as well as between blood cadmium levels and active smoking. [9] [10] [11] Also, Leroper et al. [12] and Lee et al. [13] have proven the existence of a dose-response relationship in these associations, providing strong evidence that active smoking increases blood lead and cadmium levels. Ritcher et al. found that urine lead levels among adults with high second-hand smoke exposure were similar to that of smokers [14] but the study was based on the results from data adjusted only for creatinine and other various covariates that can influence the result were not considered. Furthermore, there

have only been a few studies that have revealed an association between SHS exposure and blood lead and cadmium, thus far.

This study was conducted to examine the association between SHS and blood lead and cadmium concentration while considering the possible confounding factors and to demonstrate how SHS at home and in workplaces can influence blood lead and cadmium levels differently in S. Korean women.

# METHODS

### 1. Materials and Methods

Eligible participants are shown in Figure 1. The KNHANES V (2010–2012) was a nationwide survey representing the general Korean population and included comprehensive information on the health status, health behaviors, and socio-demographic characteristics of 25,533 participants. A total of 1,490 subjects were included in this study in accordance to the eligible criteria. Because the survey data analyzed are publicly available, this study was exempt from review by the Institutional Review Board.

SHS status was assessed among lifetime never-smokers, via a self-reported questionnaire. Then the subjects were categorized into each group according to the duration of total exposure during a one day period (0, >0 to <1, and ≥1 h), the duration of exposure at home (0, >0 to <1, and ≥1 h), and the duration of exposure at workplaces (0, >0 to <1, and ≥1 h). The participants were also asked if they had cohabiting family members who actively smoked (yes/no)

The urinary cotinine excretion is an index that reflects the degree of exposure to SHS as well as direct smoking. For the Korean National Health and Nutrition Examination Survey, urinary cotinine excretion was analyzed using a Gas Chromatograph/Mass Spectrometer (GC/MS) from Perkin Elmer Clarus 600T (PerkinElmer/Finland), which has a detection threshold of 0.28 ng/mL. While a previous study has proposed a urinary cotinine level of 50 ng/mL as the cutoff value to differentiate between active smokers and nonsmokers, [15] this value has not been validated for Asians. Kang et el. [16] suggested that a urinary cotinine level of ≥100 ng/mL was an optimal value to distinguish never-smokers from active smokers in Korean population. The sensitivity and specificity of the criteria were 94.4% and 100% respectively. Kim et al. [17] supposed that a urinary cotinine level of ≥164 ng/mL also could be used to separate never-smokers from active smokers. The sensitivity and the specificity ranged from 87.1 % to 93.8% and from 82.9% to 94.9% respectively. In our study, it was important to detect the association of SHS with lead and cadmium concentrations in the blood that was only influenced by SHS. Therefore participants with a urinary cotinine level of ≥100 ng/mL were classified as current smokers due to the criteria having a higher specificity.

Blood samples were obtained through a venipuncture, and lead and cadmium levels in the blood were measured by Graphite furnace atomic absorption spectrometry (GFAAS, AAnalyst AAS-600, Zeeman correction, Perkin Elmer, Singapore) performed by the Neodin Medical Institute. The laboratory equipment to detect blood lead and cadmium was controlled by using a standard reference material from Whole Blood Metals Control (BIO-RAD, USA) for internal quality assurance and coefficient of variation for lead and cadmium levels was kept within 10%. Additionally, external quality assurance satisfied G-EQUAS (German External Quality Assessment Scheme) which is a standard protocol to detect low dose chemical material. The detection limit of blood lead and cadmium levels from the equipment were 0.0223 ug/dL and 0.087 ug/dL respectively, and all

values detected were kept within the detection limit. [18]

The age of the subjects was limited to 19 and older. The residential area was classified based on Dong (City) and Eup (rural area) of the administrative district. Occupation was divided into three broad categories: non-employed, blue color workers and other workers. Others workers included agriculture, forestry and fishery workers, machine-operating assembly line workers and simple labor workers and the rest. Household income was divided into quartiles. Education was divided into four levels: below elementary school level, middle school graduate, high school graduate and college graduate or higher. Average daily alcohol consumption was calculated based on the total quantity per occasion and frequency of drinking in the last past year and divided into three categories: no alcohol intake, 0g-9g of alcohol, and 10g or more. Alcohol intake frequency questions (alcohol intake frequency per month and the amount of alcohol consumption per occasion) were not open answer questions so the average value for each range was applied. We converted the amount of alcohol intake to pure alcohol content (1 glass = approximately 10g).

**2. Statistical Analysis**

All analyses were performed using STATA statistical software version 13.0 (Stata Corp., College Station, TX, USA). The differences in clinical characteristics according to SHS status were assessed using unpaired t tests for the continuous variables and chi-squared tests for the discrete variables. We obtained a p value for trend across categorical variables.

We assessed the associations between self-reported SHS status and urinary cotinine concentration to evaluate whether significant discrepancies existed between them. We used an analysis of variance (ANOVA) model to determine the statistical differences in a mean urinary cotinine

according to each SHS status.

We conducted multiple linear regression analyses to calculate the adjusted means of lead and cadmium. We used the following covariates: Age, residential area (rural / urban), education level, household income, alcohol intake, and occupation. Lee and Ha [13] proved that lead and cadmium concentrations increased with age and alcohol intake in the Korean population. Shin et al. [19] showed that occupational class, family income and educational level could influence lead and cadmium concentrations in the blood for the Korean population.

All analyses were weighted to the Korean standard population from 2010 to 2012 which had reflected weights to the response rate, weights to sampling, and weights to the population structure of the KNHANES parent study. A p value <0.05 was considered significant, and we also displayed 95 % CI

# RESULTS

### Baseline characteristics

The socio-demographic characteristics and urinary cotinine concentration of the participants are presented in Table 1.

Table 1 Characteristics of study participants according to self-reported SHS exposure (n=1,490, N=9.6e+06)

| | Never-smoker without SHS exposure n=1045 N=6.5e+06, 68.1% | Never-smoker with SHS exposure n=445, N=3.0e+06, 31.9% | Odds ratio | P value |
|---|---|---|---|---|
| Age, years | 50.15 (48.74, 51.57) | 44.71 (42.40, 47.02) | | <0.001 |
| Urine cotinine, ng/mL | 5.28 (4.61, 5.96) | 8.55 (6.96, 10.13) | | <0.001 |

| | | | | |
|---|---|---|---|---|
| Residential area(%, 95% CI) | | | | 0.49 |
| Urban | 77.57 (71.64, 82.57) | 79.65 (73.04, 84,97) | 1 | |
| Rural | 22.43 (17,43, 28,36) | 20.35 (15.03, 26,96) | 0.88 | |
| Education level(%, 95% CI) | | | | 0.017 |
| ≤Elementary school | 33.79 (29.70, 38.14) | 24.86 (19.22, 31.50) | 1 | |
| Middle school | 11.13 (8.92, 13.81) | 10.48 (7.38, 14.69) | 1.28 | 0.38 |
| High school | 28.98 (25.49, 32,73) | 39.12 (33.49, 45.05) | 1.84 | 0.004 |
| ≥College | 26.10 (23.04, 29.41) | 25.54 (21.10, 30.56) | 1.33 | 0.19 |
| Family income(%, 95% CI) | | | | 0.011 |
| 1Q(low) | 24.79 (20.93, 29.11) | 19.33 (14.11, 25.89) | 1 | |
| 2Q | 26.92 (23.53, 30.61) | 21.15 (16.93, 26.11) | 1.01 | 0.97 |
| 3Q | 22.83 (19.91, 26.05) | 32.78 (27.37, 38.70) | 1.84 | 0.013 |
| 4Q | 25.45 (21.79, 29.50) | 26.73 (22.14, 31.88) | 1.35 | 0.20 |
| Daily alcohol intake(%, 95% CI) | | | | <0.001 |
| 0(nondrinker) | 42.02 (37.64, 46.54) | 26.41 (20.86, 32.82) | 1 | |
| 0-9g | 54.06 (49.74, 58.33) | 62.40 (55.94, 68.45) | 1.84 | 0.001 |
| ≥10g | 3.91 (2.77, 5.49) | 11.19 (7.92, 15.58) | 4.55 | <0.001 |
| Occupational class(%, 95% CI) | | | | <0.001 |
| non-employed | 57.84 (53.49, 62.07) | 24.10 (18.69, 30.49) | 1 | |
| Blue collar | 17.23 (13.50, 21.74) | 25.40 (19.69, 32.12) | 3.54 | <0.001 |
| others | 24.93 (22.12, 27.97) | 50.49 (43.90, 57.07) | 4.86 | <0.001 |

Data are presented as the means and 95% CI or percentages and 95% CI

SHS secondhand smoke

p value from ttest for continuous varibles or chi-squared test for categorical variables

Among the total number of participants, 31.9 % had been exposed to SHS. The mean age of the SHS-exposed group was significantly lower than that of the SHS-nonexposed group (p<0.001). The mean urinary cotinine concentration of the SHS-exposed group was significantly higher than that of the SHS-nonexposed group (p<0.001). Residential area was not statistically different between the two groups. There were no consistent trends between educational level or family income and increased exposure to SHS. However, compared to participants with an educational level of elementary school or with the first quartile of family income, participants with an educational level of high school or with the third quartile of family income had higher tendency to be exposed to SHS exposure with statistical significance (OR 1.84, p-value 0.004 and OR 1.84,

p-value 0.013 respectively). We found a consistent increase of SHS exposure as the amount of daily alcohol intake increased (p<0.001). Compared to participants who were not employed, blue-collar workers and non-blue-collar workers had higher tendency to be exposed to SHS with statistical significance.

**Urinary cotinine concentration and self-reported secondhand smoke status.**

Table 2 shows the total duration of SHS exposure was related to urinary cotinine (p<0.001).

Table 2 Urinary cotinine concentration in relation to self-reported SHS environment

| Variables | n | N | Cotinine level | p value |
|---|---|---|---|---|
| Total duration of passive smoking per day(h) | 1490 | 9.6E+06 | | <0.001 |
| 0 | 1045 | 6.5E+06 | 5.28(0.34) | |
| >0 to <1 | 287 | 1.9E+06 | 7.41(0.77) | |
| ≥1 | 158 | 1.1E+06 | 10.46(1.62) | |
| Duration of passive smoking at work per day(h) | 1490 | 9.6E+06 | | 0.007 |
| 0 | 1178 | 7.6E+06 | 5.62(0.33) | |
| >0 to <1 | 239 | 1.5E+06 | 8.44(1.15) | |
| ≥1 | 73 | 4.9E+05 | 10.77(2.18) | |
| Duration of passive smoking at home per day(h) | 1490 | 9.6E+06 | | 0.005 |
| 0 | 1284 | 7.9E+06 | 5.75(0.35) | |
| >0 to <1 | 171 | 1.3E+06 | 9.11(1.45) | |
| ≥1 | 35 | 2.8E+05 | 9.38(1.55) | |
| Presence of family members who actively smoked | 1490 | | | |
| No | 1235 | 7.6E+06 | 5.65(0.35) | 0.002 |
| Yes | 255 | 1.9E+06 | 9.02(1.07) | |

Data are presented as the means(standard error)
n unweighted sample size, N weighted sample size
p value from ANOVA
p value from t-test
ref reference value

The duration of exposure, both at work and at home, was related to urinary cotinine (p=0.007 for at work; p=0.005 for at home). Participants with cohabiting family members who actively smoked had a higher mean urinary cotinine concentration (9.02 ng/mL) than that of controls (5.65 ng/mL)

with statistical significance.

**Lead and cadmium concentration according to self-reported secondhand smoke status**

Table 3 shows lead and cadmium concentrations in the blood compared to the duration of exposure to SHS.

Table 3 Association between self-reported SHS exposure and blood concentration of lead/cadmium in never smokers

| Variables | Number | | Lead (ug/dL) | | | | Cadmium (ug/L) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | N* | Crude mean | p value | Adjusted mean | p value | *Crude mean* | p value | Adjusted mean | p value |
| Total duration of passive smoking per day(h) | 1490 | 9.6E+06 | | 0.71 (overall) | | 0.55 (overall) | | 0.313 (overall) | | 0.006 (overall) |
| 0 | 1045 | 6.5E+06 | 2.02 (1.95, 2.08) | ref | 1.97 (1.91, 2.04) | ref | 1.26 (1.21, 1.31) | ref | 1.21 (1.16, 1.25) | ref |
| >0 to <1 | 287 | 1.9E+06 | 1.95 (1.84, 2.06) | 0.31 | 1.96 (1.86, 2.07) | 0.84 | 1.08 (1.01, 1.16) | <0.001 | 1.13 (1.06, 1.19) | 0.049 |
| ≥1 | 158 | 1.1E+06 | 2.09 (1.97, 2.21) | 0.3 | 2.03 (1.91, 2.16) | 0.41 | 1.45 (1.32, 1.60) | 0.01 | 1.46 (1.35, 1.58) | <0.001 |
| Duration of passive smoking at work per day(h) | 1490 | 9.6E+06 | | 0.16 (overall) | | 0.10 (overall) | | 0.30 (overall) | | 0.005 (overall) |
| 0 | 1178 | 7.6E+06 | 2.00 (1.93, 2.06) | ref | 1.96 (1.90, 2.16) | ref | 1.25 (1.20, 1.29) | ref | 1.20 (1.16, 1.24) | ref |
| >0 to <1 | 239 | 1.5E+06 | 2.02 (1.92, 2.13) | 0.69 | 2.04 (1.93, 2.15) | 0.18 | 1.16 (1.07, 1.25) | 0.096 | 1.24 (1.15, 1.34) | 0.44 |
| ≥1 | 73 | 4.9E+05 | 2.19 (1.98, 2.40) | 0.087 | 2.11 (1.90, 2,32) | 0.18 | 1.50 (1.32, 1.68) | 0.009 | 1.50 (1.32, 1.68) | 0.001 |
| Duration of passive smoking at home per day(h) | 1490 | 9.6E+06 | | 0.45 (overall) | | 0.63 (overall) | | 0.44 (overall) | | 0.13 (overall) |
| 0 | 1284 | 7.9E+06 | 2.02 (1.96, 2.08) | ref | 1.98 (1.93, 2.04) | ref | 1.24 (1.20, 1.29) | ref | 1.21 (1.17, 1.25) | ref |
| >0 to <1 | 171 | 1.3E+06 | 1.98 (1.85, 2.10) | 0.53 | 1.98 (1.85, 2.10) | 0.93 | 1.21 (1.10, 1.32) | 0.55 | 1.23 (1.13, 1.33) | 0.74 |
| ≥1 | 35 | 2.8E+05 | 1.96 (1.71, 2.22) | 0.66 | 1.90 (1.66, 2.14) | 0.5 | 1.50 (1.18, 1.83) | 0.13 | 1.45 (1.23, 1.67) | 0.04 |
| Presence of family members who actively smoked | 1490 | 9.6E+06 | | | | | | | | |
| No | 1235 | 7.6E+06 | 2.02 (1.96, 2.09) | 0.3 | 1.98 (1.93, 2.04) | 0.79 | 1.25 (1.21, 1.30) | 0.77 | 1.21 (1.17, 1.25) | 0.43 |
| Yes | 255 | 1.9E+06 | 1.96 (1.86, 2.07) | | 1.97 (1.86, 2.08) | | 1.23 (1.13, 1.33) | | 1.25 (1.17, 1.33) | |

All data are weighted to the residential population of S.Korea (n unweighted sample size, N weighted sample size).

Multiple linear analyses were used to calculate means adjusted for age, residential area, education, family income, daily alcohol intake, and occupation

Data are presented as the means (95% CI)

p value from multivariate linear regression

ref reference value

No difference was observed in lead concentration according to SHS status, which was classified by the duration of exposure at workplaces, exposure at home and total exposure. However, cadmium concentration in the blood differed depending on the exposure status. Compared to participants who were never-exposed to SHS, participants who were exposed to SHS longer than 1 hour at work, home and total exposure demonstrated a higher cadmium concentration (1.20 vs 1.50 with p-value 0.001 ; 1.21 vs 1.45 with p-value 0.04 ; 1.21 vs 1.46 with p-value <0.0001) . We found a consistent increase in cadmium concentration as the time of SHS exposure at work increased (1.20 ug/L, 1.24 ug/L and 1.50 ug/L, p=0.005). No difference was found in lead and cadmium concentrations between participants living with active smokers and participants living without active smokers (p=0.79 for lead and p=0.43 for cadmium after adjusted for covariates)

## DISCUSSION

In this study, we have demonstrated a significant association between blood cadmium concentration and SHS exposure in a large nationally representative sample. From an adjusted analysis, we found a consistent increase of blood cadmium concentration among participants who were exposed to SHS at workplaces. Additionally, we found that participants who were exposed to SHS for a longer duration than 1 hour at home and at total exposure had higher blood cadmium concentration compared to participants who were never exposed to SHS. After adjusting for confounding factors that could influence blood concentration of the metals, we confirmed that regression coefficients of linear regression models were increased with statistical significance in the analyses of cadmium concentration of total SHS exposure and SHS exposure at workplaces (Before adjustment , regression coefficient was 0.034 with p=0.313. After adjustment, regression coefficient was 0.084 with p=0.006; before adjustment, regression coefficient was 0.042 with p=0.30. After adjustment, regression coefficient was 0.11 with p=0.005). That means the effects of exposure to SHS on cadmium concentration in the blood became more obvious after adjusting

for confounders. No significant difference was found in the levels of lead and cadmium between participants living with smokers and those without smokers (For lead p=0.79 after adjustment, for cadmium p=0.43 after adjustment). Given the circumstances in S. Korea, participants having cohabiting smokers at home does not always suggest that they will be exposed to SHS at home. Korean smokers usually smoke outdoors such as in balconies, gardens and public outdoor places near the house, before returning into the house. Therefore, despite having cohabitants that are active smokers, participants might not be exposed to a significant amount of SHS in S. Korea.

Several previous studies support the results of this study. Exposure to cigarette smoke via active and passive smoking was found to increase blood cadmium concentration among 158 workers in Israel. [20] It was reported that urinary lead concentration was found to be increased according to SHS status in the United States' adult population. [14] In Sweden, urinary cadmium concentration correlated with urinary cotinine concentration among 23 children with asthma [21]

Studies on the relationship between SHS and lead concentrations in the blood were mainly conducted with the participation of children as research subjects. It was found that lead concentrations in the blood increased as the numbers of smokers at home increased. [22] Richter et. al.[23] analyzed the blood lead level using NHANES 1999-2008 and found that higher exposure to SHS resulted in higher blood lead concentration. However, the result was more prominent in children and adolescents than in adults. In our study, we could not find any association between lead concentration in the blood and SHS exposure status. This may be the case because the average age of our study population was much older than adolescents or children. (44.71 for those who were never-exposed to SHS; 50.15 for those who were exposed to SHS)

Cadmium can enter the body through ingestion, inhalation, and the skin. Between 10 and 50% of inhaled cadmium can be absorbed and between 5 and 10% of ingested cadmium can be absorbed. The absorption of cadmium through the skin is negligible. The average cadmium concentration in the blood is twice as high in smokers than in non-smokers. [24] Korean FDA (Food and Drug Administration) investigated the concentration of metals in foods available in S. Korea . It announced that the total cadmium intake through all available foods was 10.4 μg/day, which was 22.7% of PTMI (Provisional Tolerable Weekly Intake). Grain attributed most to cadmium concentration, which was 22.9% of the total cadmium intake. Daily intake of cadmium in S. Korea was similar to that in the United States, Britain, France and Germany, but lower than that in Japan, Australia, and New Zealand. [25] In S. Korea, cadmium exposure over the age of 10 were lower than the level recommended by Center for Disease Control (CDC), Commission on Human Biological Monitoring (CHBM), World Health Organization(WHO) and Environmental Protection Agency (EPA). [26] Therefore, additional exposure to cadmium, by direct or passive smoking, is critical because it can increase the risk in disease processes caused by the metal which could be preventable. Cadmium is classified as a human carcinogen by the Interactional Agency for Research on Cancer. Cadmium may be one of the risk factors for cardiovascular mortality and the deterioration of renal function. Moreover, it is critical for post- and pre-menopausal women because osteoporosis, osteomalacia and bone fracture caused by cadmium occur mainly among postmenopausal women, in addition to potential teratogenicity. [24 27].

S. Korea has not implemented comprehensive ban on indoor smoking in public places and workplaces as recommended in the FCTC (Framework Convention on Tobacco Control) Guidelines. Smoking indoors in workplaces has decreased from 47% of smokers in 2005 to 32% in 2010. However, the decrease was less significant compared to other countries where smoking in workplaces has decreased to less than 10% after implementation of ban on indoor smoking. The

level of observed smoking in indoor workplaces was higher than other high-income ITC (International Tobacco Control) countries such as the United States, France, Canada, Ireland, and Australia, and higher than middle-income ITC countries, such as Mexico, Malaysia, and Brazil. [28] Furthermore, ban on smoking in homes has been significantly less implemented in S. Korea than in the Unites States. [29] Cadmium is especially harmful to women due to its potential catastrophic effects to the fetus. Thus, an emphasis must be placed on a social dimension regarding the dangers of SHS in order to prevent not only cancer, cardiovascular diseases, and respiratory diseases but also increased concentration of cadmium in the blood.

**Limitations**

Our study has several limitations. First, people who work in areas with higher chance of exposure to lead and cadmium were not considered. However the number of women who work in such areas is very low in Korea that it is unlikely to have an effect on the research. Second, the survey was not conducted on metals intake through the consumption of food. Although daily consumption of cadmium and lead through food is low in S. Korea, further studies are needed to show their exact relationships.

Despite these limitations, our study has several strengths. We evaluated a nationally representative sample so that the results of our study reflect characteristics of general non-smoking female population in S. Korea. Additionally, we compared the exposure between home and workplace, which have not been evaluated concurrently in previous studies.

**Conclusions**

In this study, we showed that women had elevated blood cadmium levels with increased exposure level to SHS, and there was a correlation between blood cadmium levels and the exposure level to SHS at work. This suggests that we need to further evaluate the effect of reduced exposure to SHS on the levels of cadmium in the blood. Even low blood levels of accumulated metals can be harmful to the human body. This study suggests the need for social and political efforts to reduce SHS exposure to promote healthy workplaces for women.

## CONFLICT OF INTEREST

All authors declare that they have no conflict of interest.

## ACKNOWLEGEMENT

We thank the members of the Korea Institute for Health and Social Affairs who conducted the national survey and everyone who contributed to this project. This study was supported by a grant (no. 02-2013-094) from the Seoul National University Bundang Hospital Research Fund.

## REFERENCES

1. National Center for Chronic Disease P, Health Promotion Office on S, Health. Reports of the Surgeon General. The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General. Atlanta (GA): Centers for Disease Control and Prevention (US), 2014.
2. Choi SH. Smoking status of adults and adolescents in Korea. Secondary Smoking status of adults and adolescents in Korea 2011. http://www.cdc.go.kr/CDC/cms/content/84/21484_view.html.
3. Choi S, Park S, Lee J, et al. Trends in cigarette smoking among adolescents and adults in South Korea. Epidemiol Health 2014;**36**(1):e2014023.

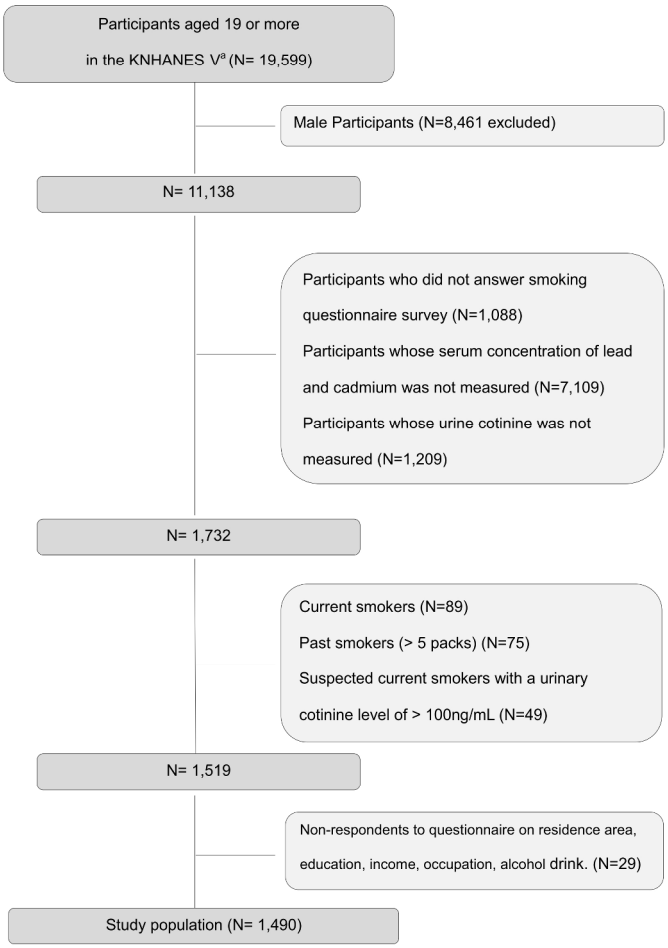
4. Cho HJ. The Status and Future Challenges of Tobacco Control Policy in Korea. Journal of preventive medicine and public health = Yebang Uihakhoe chi 2014;**47**(3):129-35.
5. Narkowicz S, Polkowska Ż, Kiełbratowska B, et al. Environmental tobacco smoke: Exposure, health effects, and analysis. Critical Reviews in Environmental Science and Technology 2013;**43**(2):121-61.
6. Health UDo, Services H. The health consequences of involuntary exposure to tobacco smoke: a report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health 2006;**709**.
7. Werler MM. Teratogen update: smoking and reproductive outcomes. Teratology 1997;**55**(6):382-8.
8. Thompson J, Bannigan J. Cadmium: toxic effects on the reproductive system and the embryo. Reproductive toxicology (Elmsford, NY) 2008;**25**(3):304-15.
9. Brockhaus A, Freier I, Ewers U, et al. Levels of cadmium and lead in blood in relation to smoking, sex, occupation, and other factors in an adult population of the FRG. International archives of occupational and environmental health 1983;**52**(2):167-75.
10. Elinder CG, Kjellstrom T, Lind B, et al. Cadmium exposure from smoking cigarettes: variations with time and country where purchased. Environmental research 1983;**32**(1):220-7.
11. Watanabe T, Kasahara M, Nakatsuka H, et al. Cadmium and lead contents of cigarettes produced in various areas of the world. The Science of the total environment 1987;**66**:29-37.
12. Leroyer A, Hemon D, Nisse C, et al. Environmental exposure to lead in a population of adults living in northern France: lead burden levels and their determinants. The Science of the total environment 2001;**267**(1-3):87-99.
13. Lee B, Ha J. The Effects of Smoking and Drinking on Blood Lead and Cadmium Levels: Data from the Fourth Korea National Health and Nutrition Examination Survey. Korean J Occup Environ Med 2011;**23**(1):31-41.
14. Richter PA, Bishop EE, Wang J, et al. Tobacco smoke exposure and levels of urinary metals in the U.S. youth and adult population: the National Health and Nutrition Examination Survey (NHANES) 1999-2004. International journal of environmental research and public health 2009;**6**(7):1930-46.
15. Goniewicz ML, Eisner MD, Lazcano-Ponce E, et al. Comparison of urine cotinine and the tobacco-specific nitrosamine metabolite 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and their ratio to discriminate active from passive smoking. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 2011;**13**(3):202-8.
16. Kang YH, Lee YJ, Kim HK, et al. Usefulness of Urinary Cotinine Test to Distinguish Smokers from Nonsmokers. Korean J Lab Med 2003;**23**(2):92-97.

17. Kim S, Jung A. Optimum cutoff value of urinary cotinine distinguishing South Korean adult smokers from nonsmokers using data from the KNHANES (2008-2010). Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 2013;**15**(9):1608-16.
18. Lee B, Ha J. The effects of smoking and drinking on blood lead and cadmium levels: data from the fourth Korea national health and nutrition examination survey. Occupational and Environmental Medicine 2011;**68**(Suppl 1):A93-A93.
19. Shin J-Y, Kim J-M, Kim Y. The association of heavy metals in blood, fish consumption frequency, and risk of cardiovascular diseases among Korean adults: The Korean National Health and Nutrition Examination Survey (2008-2010). Korean J Nutr 2012;**45**(4):347-61.
20. Shaham J, Meltzer A, Ashkenazi R, et al. Biological monitoring of exposure to cadmium, a human carcinogen, as a result of active and passive smoking. Journal of occupational and environmental medicine / American College of Occupational and Environmental Medicine 1996;**38**(12):1220-8.
21. Willers S, Gerhardsson L, Lundh T. Environmental tobacco smoke (ETS) exposure in children with asthma—relation between lead and cadmium, and cotinine concentrations in urine. Respiratory Medicine 2005;**99**(12):1521-27.
22. Apostolou A, Garcia-Esquinas E, Fadrowski JJ, et al. Secondhand tobacco smoke: a source of lead exposure in US children and adolescents. American journal of public health 2012;**102**(4):714-22.
23. Richter PA, Bishop EE, Wang J, et al. Trends in tobacco smoke exposure and blood lead levels among youths and adults in the United States: the National Health and Nutrition Examination Survey, 1999-2008. Preventing chronic disease 2013;**10**:E213.
24. Nordberg GF, Fowler BA, Nordberg M, et al. *Handbook on the Toxicology of Metals*: Academic Press, 2011.
25. Kim SH. Investigation of food metals in food and risk asseement in S.Korea. Secondary Investigation of food metals in food and risk asseement in S.Korea 2011. http://m.mfds.go.kr/jsp/livinginfo_v.jsp?site_code=1&board_code=31&seq=16682&page=31&searchText=.
26. Roh SJ. Concentration of blood heavy metal monitoring in the fifth Korea National Health and Nutrition Examination Survey(KNHANES, 2010). Secondary Concentration of blood heavy metal monitoring in the fifth Korea National Health and Nutrition Examination Survey(KNHANES, 2010) 2010.
27. Kim KH, Lee CM, Park SM, et al. Secondhand smoke exposure and osteoporosis in never-smoking postmenopausal women: the Fourth Korea National Health and Nutrition Examination Survey. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 2013;**24**(2):523-32.
28. Seo HG. ITC Korea National Report Waves 1 to 3 (2005-2010). Secondary ITC Korea National

Report Waves 1 to 3 (2005-2010) 2012. http://www.itcproject.org/resources/view/1139.

29. Ayers JW, Hofstetter CR, Hughes SC, et al. Smoking on both sides of the pacific: home smoking restrictions and secondhand smoke exposure among Korean adults and children in Seoul and California. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 2010;**12**(11):1142-50.

Figure 1. Study population




210x297mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract : page 2 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found : page 2 |
| **Introduction** | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported : pages 3-4 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses : page 4 |
| **Methods** | | |
| Study design | 4 | Present key elements of study design early in the paper: pages 4-6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection : pages 4-5 |
| Participants | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed<br>*Case-control study*—For matched studies, give matching criteria and the number of controls per case: pages 4-5 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable : pages 4-7 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group : pages 4-6 |
| Bias | 9 | Describe any efforts to address potential sources of bias: page 15 |
| Study size | 10 | Explain how the study size was arrived at: page 4 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why: page 7 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding: page 7 |
| | | (*b*) Describe any methods used to examine subgroups and interactions: page 7 |
| | | (*c*) Explain how missing data were addressed: page 7 |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed<br>*Case-control study*—If applicable, explain how matching of cases and controls was addressed<br>*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy: page 7 |
| | | (*e*) Describe any sensitivity analyses |

Continued on next page

| | | |
|---|---|---|
| **Results** | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed: pages 7-12 |
| | | (b) Give reasons for non-participation at each stage: pages 7-12 |
| | | (c) Consider use of a flow diagram: pages 7-12 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders: pages 7-12 |
| | | (b) Indicate number of participants with missing data for each variable of interest: pages 7-12 |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) : pages 7-12 |
| Outcome data | 15* | *Cohort study*—Report numbers of outcome events or summary measures over time |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures: pages 7-12 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included: pages 7-12 |
| | | (*b*) Report category boundaries when continuous variables were categorized: pages 7-12 |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |
| **Discussion** | | |
| Key results | 18 | Summarise key results with reference to study objectives: pages 12-16 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias: pages 12-16 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence: pages 12-16 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results: pages 12-16 |
| **Other information** | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based: page 16 |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

# The association between secondhand smoke exposure and blood lead and cadmium concentration in community dwelling women: The fifth Korea National Health and Nutrition Examination Survey (2010-2012)



| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID: | bmjopen-2015-008218.R1 |
| Article Type: | Research |
| Date Submitted by the Author: | 26-Jun-2015 |
| Complete List of Authors: | Jung, Se Young; Seoul National University Bundang Hospital, Seoul National University College of Medicine, Department of Family Medicine<br>Kim, Suyeon; Seoul National University Hospital, Department of Family Medicine<br>Lee, Kiheon ; Seoul National University Bundang Hospital, Seoul National University College of Medicine, Department of Family Medicine<br>Kim, Joo Young; Seoul National University Bundang Hospital, Seoul National University College of Medicine, Department of Family Medicine<br>Bae, Woo Kyung; Seoul National University Bundang Hospital, Health Promotion Center<br>Lee, Keehyuck; Seoul National University Bundang Hospital, Seoul National University College of Medicine, Department of Family Medicine<br>Han, Jong-Soo; Seoul National University Bundang Hospital, Health Promotion Center<br>Kim, Sarah; Seoul National University Bundang Hospital, Seoul National University College of Medicine, Department of Family Medicine |
| Primary Subject Heading: | Smoking and tobacco |
| Secondary Subject Heading: | Addiction, Health policy, Occupational and environmental medicine, Public health, General practice / Family practice |
| Keywords: | TOXICOLOGY, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, OCCUPATIONAL & INDUSTRIAL MEDICINE, PRIMARY CARE |
| | |

# The association between secondhand smoke exposure and blood lead and cadmium concentration in community dwelling women: The fifth Korea National Health and Nutrition Examination Survey (2010-2012)

**Authors:** Se Young Jung[1], Suyeon Kim[2], Kiheon Lee[3*], Joo Young Kim[4], Woo Kyung Bae[5], Keehyuck Lee[6], Jong-Soo Han[7], Sarah Kim[8]

**Affiliation(s) of authors**

**1,3,4,6,8** Department of Family Medicine, Seoul National University College of Medicine and Seoul National University Bundang Hospital, Seongnam, Korea

**2** Department of Family Medicine, Seoul National University Hospital, Seoul, Korea,

**5, 7** Health Promotion Center, Seoul National University Bundang Hospital**,** Seongnam, Korea

**S. Y. Jung and S. Kim contributed equally to this work as first authors.**

**The e-mail address, telephone and fax numbers of the corresponding author**

82, Gumi-ro, 173 beon-gil, Bundang-gu, Seongnam-si, Gyeongi-do, Korea, Postal code: 463-707

Telephone: 82-31-787-7809, Fax: 82-31-787-4014, E-mail: keyhoney@gmail.com,

**Word count: 3,025**

**Key words:** Secondhand smoke, Lead, Cadmium, Metals, Workplace

## ABSTRACT

**Objectives:** To assess the association between secondhand smoke exposure and blood lead and cadmium concentration in women in S. Korea.

**Design:** Population-based cross-sectional study

**Setting:** South Korea **(**Korea National Health and Nutrition Examination Survey V)

**Participants:** 1,490 non-smoking women who took part in the fifth Korea National Health and Nutrition Examination Survey (2010-2012), in which blood levels of lead and cadmium were measured.

**Primary outcome measures:** The primary outcome were blood levels of lead and cadmium in

accordance to the time of secondhand smoke exposure.

**Results:** The adjusted mean level of blood cadmium in women who were never exposed to secondhand smoking per day was 1.21(0.02)ug/L. Among women who were exposed less than 1 hour per day, the mean cadmium level was 1.13(0.03)ug/L, and for those exposed for more than 1 hour, the mean level was 1.46(0.06)ug/L. In particular, there was a significant association between duration of secondhand smoking and blood cadmium concentration at workplace. The adjusted means of blood cadmium concentration in women who never exposed group, less than 1 hour exposed groups and more than 1 hour exposed group at workplace were 1.20ug/L, 1.24ug/L, 1.50ug/L, respectively. We could not find any association between lead concentration in the blood and secondhand smoke exposure status.

**Conclusions:** This study showed that exposure to secondhand smoke and blood cadmium levels are associated. Especially, there was a significant association at workplace. Therefore, social and political efforts for reducing the exposure to secondhand smoke at workplace are needed in order to promote a healthier working environment for women

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first study to show that women have elevated blood cadmium levels with increased exposure level to SHS, and there is a correlation between blood cadmium levels and the exposure level to SHS at work.

- We evaluated a nationally representative sample so that the results of our study reflect characteristics of general non-smoking female population in S. Korea.

- We compared the exposure between home and workplace, which have not been evaluated concurrently in previous studies.

- Out study has several weaknesses: First, people who work in areas with higher chance of exposure to lead and cadmium were not considered. However the number of women who work in such areas is very low in S. Korea that it is unlikely to have an effect on the research. Second, the survey was not conducted on metals intake through the consumption of food. However, daily consumption of cadmium and lead through food is low in S. Korea

# INTRODUCTION

Exposures to secondhand smoking (SHS) has been a particular public health concern as it is causally linked to lung cancer, stroke, coronary heart disease, nasal irritation and reproductive harmful effects in women. [1] There has been significant progress to reduce SHS exposure. However, nearly half (46.4%) of nonsmokers in the United States remain exposed. [1] In S. Korea, 4.9% of men and 16.7% of women were exposed to SHS at home and 55.2% of men and 37.2% of women were exposed to SHS at workplaces in 2011. [2 3] Overall, more than 30% of non-smoking adults and adolescents are still exposed to secondhand smoke in 2014. [4] Smoke-free policies have shown incremental progress since 1995, but smoking is still permitted in many indoor public places. [4]

Cigarette smoke consists of mainstream smoke from the mouth ends of cigarettes during puffing and sidestream smoke from the lit ends of the cigarettes between puffs. The sidestream smoke can reach deeper areas in the lung because the size and concentration of the particle are smaller and higher, respectively, than that of mainstream smoke. SHS is a mixture of the sidestream smoke and exhaled mainstream smoke [5] and contains more than 4000 chemical compounds known to cause diseases, including nitrosamines, polycyclic aromatic hydrocarbons (PAHs), cadmium, chromium, lead and nickel [5 6] Lead and cadmium have been particular concerns due to their carcinogenicity, tendency to accumulate in the body and their potential toxicity to the developing fetus [7 8]

There are strong associations between the blood lead levels and active smoking, as well as between blood cadmium levels and active smoking. [9 10 11] Also, Leroper et al. [12] and Lee et al. [13] have proven the existence of a dose-response relationship in these associations, providing strong evidence that active smoking increases blood lead and cadmium levels. Ritcher et al. found that urine lead levels among adults with high second-hand smoke exposure were similar to that of smokers [14] but the study was based on the results from data adjusted only for creatinine and other various covariates that can influence the result were not considered. Furthermore, there have only been a few studies that have revealed an association between SHS exposure and blood lead and cadmium, thus far.

This study was conducted to examine the association between SHS and blood lead and cadmium concentration while considering the possible confounding factors and to demonstrate how SHS at home and in workplaces can influence blood lead and cadmium levels differently in S. Korean women.

# METHODS

## 1. Materials and Methods

Eligible participants are shown in Figure 1. The KNHANES V (2010–2012) was a nationwide survey representing the general Korean population and included comprehensive information on the health status, health behaviors, and socio-demographic characteristics of 25,533 participants. A total of 1,490 subjects were included in this study in accordance to the eligible criteria. The KNHANES V used a stratified multistage probability sampling so that the sampled population accurately represents the general population of Korea. A total of 1,490 subjects represented 9,600,000 Korean population. Because the survey data analyzed are publicly available, this study was exempt from review by the Institutional Review Board.

SHS status was assessed among lifetime never-smokers, via a self-reported questionnaire. Then the subjects were categorized into each group according to the duration of total exposure during a one day period (0, >0 to <1, and ≥1 h), the duration of exposure at home (0, >0 to <1, and ≥1 h), and the duration of exposure at workplaces (0, >0 to <1, and ≥1 h). The participants were also asked if they had cohabiting family members who actively smoked (yes/no)

The urinary cotinine excretion is an index that reflects the degree of exposure to SHS as well as direct smoking. For the Korean National Health and Nutrition Examination Survey, urinary cotinine excretion was analyzed using a Gas Chromatograph/Mass Spectrometer (GC/MS) from Perkin Elmer Clarus 600T (PerkinElmer/Finland), which has a detection threshold of 0.28 ng/mL. While a previous study has proposed a urinary cotinine level of 50 ng/mL as the cutoff value to differentiate between active smokers and nonsmokers, [15] this value has not been validated for Asians. Kang et el. [16] suggested that a urinary cotinine level of ≥100 ng/mL was an optimal value to distinguish never-smokers from active smokers in Korean population. The sensitivity and specificity of the criteria were 94.4% and 100% respectively. Kim et al. [17] supposed that a urinary cotinine level of ≥164 ng/mL also could be used to separate never-smokers from active smokers. The sensitivity and the specificity ranged from 87.1 % to 93.8% and from 82.9% to 94.9% respectively. In our study, it was important to detect the association of SHS with lead and cadmium concentrations in the blood that was only influenced by SHS. Therefore participants with a urinary cotinine level of ≥100 ng/mL were classified as current smokers due to the criteria having a higher specificity. In this study, current and past smokers were excluded through interviews and suspected current smokers, whose urinary cotinine concentration was above 100 ng/mL were also excluded.

Blood samples were obtained through a venipuncture, and lead and cadmium levels in the blood were measured by Graphite furnace atomic absorption spectrometry (GFAAS, AAnalyst AAS-600, Zeeman correction, Perkin Elmer, Singapore) performed by the Neodin Medical Institute. The laboratory equipment to detect blood lead and cadmium was controlled by using a standard reference material from Whole Blood Metals Control (BIO-RAD, USA) for internal quality assurance and coefficient of variation for lead and cadmium levels was kept within 10%. Additionally, external quality assurance satisfied G-EQUAS (German External Quality Assessment Scheme) which is a standard protocol to detect low dose chemical material. The detection limit of blood lead and cadmium levels from the equipment were 0.0223 ug/dL and 0.087 ug/dL respectively, and all values detected were kept within the detection limit. [18]

The age of the subjects was limited to 19 and older. The residential area was classified based on Dong (City) and Eup (rural area) of the administrative district. Occupation was divided into three broad categories: non-employed, blue color workers and other workers. Others workers included agriculture, forestry and fishery workers, machine-operating assembly line workers and simple labor workers and the rest. Household income was divided into quartiles. Education was divided into four levels: below elementary school level, middle school graduate, high school graduate and college graduate or higher. Average daily alcohol consumption was calculated based on the total quantity per occasion and frequency of drinking in the last past year and divided into three categories: no alcohol intake, 0g-9g of alcohol, and 10g or more. Alcohol intake frequency questions (alcohol intake frequency per month and the amount of alcohol consumption per occasion) were not open answer questions so the average value for each range was applied. We converted the amount of alcohol intake to pure alcohol content (1 glass = approximately 10g).

**2. Statistical Analysis**

All analyses were performed using STATA statistical software version 13.0 (Stata Corp., College Station, TX, USA). The differences in clinical characteristics according to SHS status were assessed using unpaired t tests for the continuous variables and chi-squared tests for the discrete variables. We obtained a p value for trend across categorical variables.

We assessed the associations between self-reported SHS status and urinary cotinine concentration to evaluate whether significant discrepancies existed between them. We used an analysis of variance (ANOVA) model to determine the statistical differences in a mean urinary cotinine according to each SHS status.

We conducted multiple linear regression analyses to calculate the adjusted means of lead and cadmium. We used the following covariates: Age, residential area (rural / urban), education level, household income, alcohol intake, and occupation. Lee and Ha [13] proved that lead and cadmium concentrations increased with age and alcohol intake in the Korean population. Shin et al. [19] showed that occupational class, family income and educational level could influence lead and cadmium concentrations in the blood for the Korean population.

All analyses were weighted to the Korean standard population from 2010 to 2012 which had reflected weights to the response rate, weights to sampling, and weights to the population structure of the KNHANES parent study. A p value <0.05 was considered significant, and we also displayed 95 % CI

# RESULTS

### Baseline characteristics

The socio-demographic characteristics and urinary cotinine concentration of the participants are presented in Table 1.

Table 1 Characteristics of study participants according to self-reported SHS exposure (n=1,490, N=9.6e+06)

| | Never-smoker without SHS exposure n=1045, 68.1% | Never-smoker with SHS exposure n=445, 31.9% | P value |
|---|---|---|---|
| Age, years | 50.15 (48.74, 51.57) | 44.71 (42.40, 47.02) | <0.001 |
| Urine cotinine, ng/mL | 5.28 (4.61, 5.96) | 8.55 (6.96, 10.13) | <0.001 |
| Residential area(%, 95% CI) | | | 0.49 |
| Urban | 77.57 (71.64, 82.57) | 79.65 (73.04, 84,97) | |
| Rural | 22.43 (17,43, 28,36) | 20.35 (15.03, 26,96) | |
| Education level(%, 95% CI) | | | 0.017 |
| ≤Elementary school | 33.79 (29.70, 38.14) | 24.86 (19.22, 31.50) | |
| Middle school | 11.13 (8.92, 13.81) | 10.48 (7.38, 14.69) | 0.38 |
| High school | 28.98 (25.49, 32,73) | 39.12 (33.49, 45.05) | 0.004 |
| ≥College | 26.10 (23.04, 29.41) | 25.54 (21.10, 30.56) | 0.19 |
| Family income(%, 95% CI) | | | 0.011 |
| 1Q(low) | 24.79 (20.93, 29.11) | 19.33 (14.11, 25.89) | |
| 2Q | 26.92 (23.53, 30.61) | 21.15 (16.93, 26.11) | 0.97 |
| 3Q | 22.83 (19.91, 26.05) | 32.78 (27.37, 38.70) | 0.013 |
| 4Q | 25.45 (21.79, 29.50) | 26.73 (22.14, 31.88) | 0.20 |

| | | | |
|---|---|---|---|
| Daily alcohol intake(%, 95% CI) | | | <0.001 |
| 0(nondrinker) | 42.02 (37.64, 46.54) | 26.41 (20.86, 32.82) | |
| 0-9g | 54.06 (49.74, 58.33) | 62.40 (55.94, 68.45) | 0.001 |
| ≥10g | 3.91 (2.77, 5.49) | 11.19 (7.92, 15.58) | <0.001 |
| Occupational class(%, 95% CI) | | | <0.001 |
| non-employed | 57.84 (53.49, 62.07) | 24.10 (18.69, 30.49) | |
| Blue collar | 17.23 (13.50, 21.74) | 25.40 (19.69, 32.12) | <0.001 |
| others | 24.93 (22.12, 27.97) | 50.49 (43.90, 57.07) | <0.001 |

Data are presented as the means and 95% CI or percentages and 95% CI

SHS secondhand smoke

p value from ttest for continuous varibles or chi-squared test for categorical variables

Among the total number of participants, 31.9 % had been exposed to SHS. The mean age of the SHS-exposed group was significantly lower than that of the SHS-nonexposed group (p<0.001). The mean urinary cotinine concentration of the SHS-exposed group was significantly higher than that of the SHS-nonexposed group (p<0.001). Residential area was not statistically different between the two groups. There were no consistent trends between educational level or family income and increased exposure to SHS. However, compared to participants with an educational level of elementary school or with the first quartile of family income, participants with an educational level of high school or with the third quartile of family income had higher tendency to be exposed to SHS exposure with statistical significance (OR 1.84, p-value 0.004 and OR 1.84, p-value 0.013 respectively). We found a consistent increase of SHS exposure as the amount of daily alcohol intake increased (p<0.001). Compared to participants who were not employed, blue-collar workers and non-blue-collar workers had higher tendency to be exposed to SHS with statistical significance.

**Urinary cotinine concentration and self-reported secondhand smoke status.**

Table 2 shows the total duration of SHS exposure was related to urinary cotinine (p<0.001).

Table 2 Urinary cotinine concentration in relation to self-reported SHS environment

| Variables | n | Cotinine level | p value |
|---|---|---|---|
| Total duration of passive smoking per day(h) | 1490 | | <0.001 |
| 0 | 1045 | 5.28(0.34) | |
| >0 to <1 | 287 | 7.41(0.77) | |
| ≥1 | 158 | 10.46(1.62) | |
| Duration of passive smoking at work per day(h) | 1490 | | 0.007 |
| 0 | 1178 | 5.62(0.33) | |
| >0 to <1 | 239 | 8.44(1.15) | |

| | | | |
|---|---|---|---|
| ≥1 | 73 | 10.77(2.18) | |
| Duration of passive smoking at home per day(h) | 1490 | | 0.005 |
| 0 | 1284 | 5.75(0.35) | |
| >0 to <1 | 171 | 9.11(1.45) | |
| ≥1 | 35 | 9.38(1.55) | |
| Presence of family members who actively smoked | 1490 | | |
| No | 1235 | 5.65(0.35) | 0.002 |
| Yes | 255 | 9.02(1.07) | |

Data are presented as the means(standard error)
n unweighted sample size, N weighted sample size
p value from ANOVA
p value from t-test
ref reference value

The duration of exposure, both at work and at home, was related to urinary cotinine (p=0.007 for at work; p=0.005 for at home). Participants with cohabiting family members who actively smoked had a higher mean urinary cotinine concentration (9.02 ng/mL) than that of controls (5.65 ng/mL) with statistical significance.

**Lead and cadmium concentration according to self-reported secondhand smoke status**

Table 3 shows lead and cadmium concentrations in the blood compared to the duration of exposure to SHS.

Table 3 Association between self-reported SHS exposure and blood concentration of lead/cadmium in never smokers

| Variables | Number | Lead (ug/dL) | | | | Cadmium (ug/L) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | n | Crude mean | p value | Adjusted mean | p value | *Crude mean* | p value | Adjusted mean | p value |
| Total duration of passive smoking per day(h) | 1490 | | 0.71 (overall) | | 0.55 (overall) | | 0.313 (overall) | | 0.006 (overall) |
| 0 | 1045 | 2.02 (1.95, 2.08) | ref | 1.97 (1.91, 2.04) | ref | 1.26 (1.21, 1.31) | ref | 1.21 (1.16, 1.25) | ref |
| >0 to <1 | 287 | 1.95 (1.84, 2.06) | 0.31 | 1.96 (1.86, 2.07) | 0.84 | 1.08 (1.01, 1.16) | <0.001 | 1.13 (1.06, 1.19) | 0.049 |
| ≥1 | 158 | 2.09 (1.97, 2.21) | 0.3 | 2.03 (1.91, 2.16) | 0.41 | 1.45 (1.32, 1.60) | 0.01 | 1.46 (1.35, 1.58) | <0.001 |
| Duration of passive smoking at work per day(h) | 1490 | | 0.16 (overall) | | 0.10 (overall) | | 0.30 (overall) | | 0.005 (overall) |
| 0 | 1178 | 2.00 (1.93, 2.06) | ref | 1.96 (1.90, 2.16) | ref | 1.25 (1.20, 1.29) | ref | 1.20 (1.16, 1.24) | ref |
| >0 to <1 | 239 | 2.02 (1.92, 2.13) | 0.69 | 2.04 (1.93, 2.15) | 0.18 | 1.16 (1.07, 1.25) | 0.096 | 1.24 (1.15, 1.34) | 0.44 |
| ≥1 | 73 | 2.19 (1.98, 2.40) | 0.087 | 2.11 (1.90, 2,32) | 0.18 | 1.50 (1.32, 1.68) | 0.009 | 1.50 (1.32, 1.68) | 0.001 |
| Duration of passive smoking at home per day(h) | 1490 | | 0.45 (overall) | | 0.63 (overall) | | 0.44 (overall) | | 0.13 (overall) |
| 0 | 1284 | 2.02 (1.96, 2.08) | ref | 1.98 (1.93, 2.04) | ref | 1.24 (1.20, 1.29) | ref | 1.21 (1.17, 1.25) | ref |
| >0 to <1 | 171 | 1.98 (1.85, 2.10) | 0.53 | 1.98 (1.85, 2.10) | 0.93 | 1.21 (1.10, 1.32) | 0.55 | 1.23 (1.13, 1.33) | 0.74 |
| ≥1 | 35 | 1.96 (1.71, 2.22) | 0.66 | 1.90 (1.66, 2.14) | 0.5 | 1.50 (1.18, 1.83) | 0.13 | 1.45 (1.23, 1.67) | 0.04 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Presence of family members who actively smoked | 1490 | | | | | |
| | | 0.3 | 0.79 | 0.77 | 0.43 | |
| No | 1235 | 2.02 (1.96, 2.09) | 1.98 (1.93, 2.04) | 1.25 (1.21, 1.30) | 1.21 (1.17, 1.25) | |
| Yes | 255 | 1.96 (1.86, 2.07) | 1.97 (1.86, 2.08) | 1.23 (1.13, 1.33) | 1.25 (1.17, 1.33) | |

All data are weighted to the residential population of S.Korea

Multiple linear analyses were used to calculate means adjusted for age, residential area, education, family income, daily alcohol intake, and occupation

Data are presented as the means (95% CI)

p value from multivariate linear regression

ref reference value

No difference was observed in lead concentration according to SHS status, which was classified by the duration of exposure at workplaces, exposure at home and total exposure. However, cadmium concentration in the blood differed depending on the exposure status. Compared to participants who were never-exposed to SHS, participants who were exposed to SHS longer than 1 hour at work, home and total exposure demonstrated a higher cadmium concentration (1.20 vs 1.50 with p-value 0.001 ; 1.21 vs 1.45 with p-value 0.04 ; 1.21 vs 1.46 with p-value <0.0001) . We found a consistent increase in cadmium concentration as the time of SHS exposure at work increased (1.20 ug/L, 1.24 ug/L and 1.50 ug/L, p=0.005). No difference was found in lead and cadmium concentrations between participants living with active smokers and participants living without active smokers (p=0.79 for lead and p=0.43 for cadmium after adjusted for covariates)

## DISCUSSION

In this study, we have demonstrated a significant association between blood cadmium concentration and SHS exposure in a large nationally representative sample. From an adjusted analysis, we found a consistent increase of blood cadmium concentration among participants who were exposed to SHS at workplaces. Additionally, we found that participants who were exposed to SHS for a longer duration than 1 hour at home and at total exposure had higher blood cadmium concentration compared to participants who were never exposed to SHS. After adjusting for confounding factors that could influence blood concentration of the metals, we confirmed that regression coefficients of linear regression models were increased with statistical significance in the analyses of cadmium concentration of total SHS exposure and SHS exposure at workplaces (Before adjustment , regression coefficient was 0.034 with p=0.313. After adjustment, regression coefficient was 0.084 with p=0.006; before adjustment, regression coefficient was 0.042 with p=0.30. After adjustment, regression coefficient was 0.11 with p=0.005). That means the effects of exposure to SHS on cadmium concentration in the blood became more obvious after adjusting for confounders. No significant difference was found in the levels of lead and cadmium between participants living with smokers and those without smokers (For lead p=0.79 after adjustment, for cadmium p=0.43 after adjustment). Given the circumstances in S. Korea, participants having cohabiting smokers at home does not always suggest that they will be exposed to SHS at home. Korean smokers usually smoke outdoors such as in balconies, gardens and public outdoor places near the house, before returning into the house. Therefore, despite having cohabitants that are active smokers, participants might not be exposed to a significant amount of SHS in S. Korea.

Several previous studies support the results of this study. Tobacco is well known as a notable source of cadmium and lead. [20] Exposure to cigarette smoke via active and passive smoking was found to increase blood cadmium concentration among 158 workers in Israel. [21] It was reported that urinary lead concentration was found to be increased according to SHS status in the United States' adult population. [14]

In Sweden, urinary cadmium concentration correlated with urinary cotinine concentration among 23 children with asthma [22]

Studies on the relationship between SHS and lead concentrations in the blood were mainly conducted with the participation of children as research subjects. It was found that lead concentrations in the blood increased as the numbers of smokers at home increased. [23] Richter et. al.[24] analyzed the blood lead level using NHANES 1999-2008 and found that higher exposure to SHS resulted in higher blood lead concentration. However, the result was more prominent in children and adolescents than in adults. In our study, we could not find any association between lead concentration in the blood and SHS exposure status. This may be the case because the average age of our study population was much older than adolescents or children. (44.71 for those who were never-exposed to SHS; 50.15 for those who were exposed to SHS) This can be explained by the fact that lead exposure comes largely from the general environment including ambient air, diets and daily life activities. [25]

Cadmium can enter the body through ingestion, inhalation, and the skin. Between 10 and 50% of inhaled cadmium can be absorbed and between 5 and 10% of ingested cadmium can be absorbed. The absorption of cadmium through the skin is negligible. The average cadmium concentration in the blood is twice as high in smokers than in non-smokers. [25] Korean FDA (Food and Drug Administration) investigated the concentration of metals in foods available in S. Korea . It announced that the total cadmium intake through all available foods was 10.4 μg/day, which was 22.7% of PTMI (Provisional Tolerable Weekly Intake). Grain attributed most to cadmium concentration, which was 22.9% of the total cadmium intake. Daily intake of cadmium in S. Korea was similar to that in the United States, Britain, France and Germany, but lower than that in Japan, Australia, and New Zealand. [26] In S. Korea, cadmium exposure over the age of 10 were lower than the level recommended by Center for Disease Control (CDC), Commission on Human Biological Monitoring (CHBM), World Health Organization(WHO) and Environmental Protection Agency (EPA). [27] Therefore, additional exposure to cadmium, by direct or passive smoking, is critical because it can increase the risk in disease processes caused by the metal which could be preventable. Cadmium is classified as a human carcinogen by the Interactional Agency for Research on Cancer. Cadmium may be one of the risk factors for cardiovascular mortality and the deterioration of renal function. Moreover, it is critical for post- and pre-menopausal women because osteoporosis, osteomalacia and bone fracture caused by cadmium occur mainly among postmenopausal women, in addition to potential teratogenicity. [25 28].

S. Korea has not implemented comprehensive ban on indoor smoking in public places and workplaces as recommended in the FCTC (Framework Convention on Tobacco Control) Guidelines. Smoking indoors in

workplaces has decreased from 47% of smokers in 2005 to 32% in 2010. However, the decrease was less significant compared to other countries where smoking in workplaces has decreased to less than 10% after implementation of ban on indoor smoking. The level of observed smoking in indoor workplaces was higher than other high-income ITC (International Tobacco Control) countries such as the United States, France, Canada, Ireland, and Australia, and higher than middle-income ITC countries, such as Mexico, Malaysia, and Brazil. [29] Furthermore, ban on smoking in homes has been significantly less implemented in S. Korea than in the Unites States. [30] Cadmium is especially harmful to women due to its potential catastrophic effects to the fetus. Thus, an emphasis must be placed on a social dimension regarding the dangers of SHS in order to prevent not only cancer, cardiovascular diseases, and respiratory diseases but also increased concentration of cadmium in the blood.

**Limitations**

Our study has several limitations. First, people who work in areas with higher chance of exposure to lead and cadmium were not considered. However the number of women who work in such areas is very low in Korea that it is unlikely to have an effect on the research. Second, the accumulation of metals in the blood is a long-term process. Variables such as exposure to SHS used in this study are evaluated at the present time. This can bias the results. Third, the study was based on a self-administered questionnaire about the exposure to SHS used as a proxy variable reflecting the SHS exposure status. This can lead to biased results. Lastly, the survey was not conducted on metals intake through the consumption of food. Although daily consumption of cadmium and lead through food is low in S. Korea, further studies are needed to show their exact relationships.

Despite these limitations, our study has several strengths. We evaluated a nationally representative sample so that the results of our study reflect characteristics of general non-smoking female population in S. Korea. Additionally, we compared the exposure between home and workplace, which have not been evaluated concurrently in previous studies.

**Conclusions**

In this study, we showed that women had elevated blood cadmium levels with increased exposure level to SHS, and there was a correlation between blood cadmium levels and the exposure level to SHS at work. This suggests that we need to further evaluate the effect of reduced exposure to SHS on the levels of cadmium in the blood. Even low blood levels of accumulated metals can be harmful to the human body. This study suggests the need for social and political efforts to reduce SHS exposure to promote healthy workplaces for women.

## ACKNOWLEGEMENT

We thank the members of the Korea Institute for Health and Social Affairs who conducted the national survey and everyone who contributed to this project.

## Contributorship statement

S.Y. Jung and S. Kim designed the study, analyzed the data, and drafted the manuscript as first authors. J.Y. Kim, W.K. Bae, K.Lee, J.Han and S.Kim contributed to the discussion of data and reviewed the manuscript. K.Lee supervised the study as a corresponding author.

## Competing interest

All authors declare that they have no conflict of interest.

## Funding

This study was supported by a grant (no. 02-2013-094) from the Seoul National University Bundang Hospital Research Fund.

## Data sharing statement

KNHANES V dataset is publicly available in S.Korea and any requests for analyses can be received on the website: https://knhanes.cdc.go.kr/knhanes/index.do

## REFERENCES

1. National Center for Chronic Disease P, Health Promotion Office on S, Health. Reports of the Surgeon General. The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General. Atlanta (GA): Centers for Disease Control and Prevention (US), 2014.
2. Choi SH. Smoking status of adults and adolescents in Korea. Secondary Smoking status of adults and adolescents in Korea 2011. http://www.cdc.go.kr/CDC/cms/content/84/21484_view.html.
3. Choi S, Park S, Lee J, et al. Trends in cigarette smoking among adolescents and adults in South

Korea. Epidemiol Health 2014;**36**(1):e2014023.

4. Cho HJ. The Status and Future Challenges of Tobacco Control Policy in Korea. Journal of preventive medicine and public health = Yebang Uihakhoe chi 2014;**47**(3):129-35.
5. Narkowicz S, Polkowska Ż, Kiełbratowska B, et al. Environmental tobacco smoke: Exposure, health effects, and analysis. Critical Reviews in Environmental Science and Technology 2013;**43**(2):121-61.
6. Health UDo, Services H. The health consequences of involuntary exposure to tobacco smoke: a report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health 2006;**709**.
7. Werler MM. Teratogen update: smoking and reproductive outcomes. Teratology 1997;**55**(6):382-8.
8. Thompson J, Bannigan J. Cadmium: toxic effects on the reproductive system and the embryo. Reproductive toxicology (Elmsford, NY) 2008;**25**(3):304-15.
9. Brockhaus A, Freier I, Ewers U, et al. Levels of cadmium and lead in blood in relation to smoking, sex, occupation, and other factors in an adult population of the FRG. International archives of occupational and environmental health 1983;**52**(2):167-75.
10. Elinder CG, Kjellstrom T, Lind B, et al. Cadmium exposure from smoking cigarettes: variations with time and country where purchased. Environmental research 1983;**32**(1):220-7.
11. Watanabe T, Kasahara M, Nakatsuka H, et al. Cadmium and lead contents of cigarettes produced in various areas of the world. The Science of the total environment 1987;**66**:29-37.
12. Leroyer A, Hemon D, Nisse C, et al. Environmental exposure to lead in a population of adults living in northern France: lead burden levels and their determinants. The Science of the total environment 2001;**267**(1-3):87-99.
13. Lee B, Ha J. The Effects of Smoking and Drinking on Blood Lead and Cadmium Levels: Data from the Fourth Korea National Health and Nutrition Examination Survey. Korean J Occup Environ Med 2011;**23**(1):31-41.
14. Richter PA, Bishop EE, Wang J, et al. Tobacco smoke exposure and levels of urinary metals in the U.S. youth and adult population: the National Health and Nutrition Examination Survey (NHANES) 1999-2004. International journal of environmental research and public health 2009;**6**(7):1930-46.
15. Goniewicz ML, Eisner MD, Lazcano-Ponce E, et al. Comparison of urine cotinine and the tobacco-specific nitrosamine metabolite 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and their ratio to discriminate active from passive smoking. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 2011;**13**(3):202-8.
16. Kang YH, Lee YJ, Kim HK, et al. Usefulness of Urinary Cotinine Test to Distinguish Smokers from Nonsmokers. Korean J Lab Med 2003;**23**(2):92-97.
17. Kim S, Jung A. Optimum cutoff value of urinary cotinine distinguishing South Korean adult smokers from nonsmokers using data from the KNHANES (2008-2010). Nicotine & tobacco

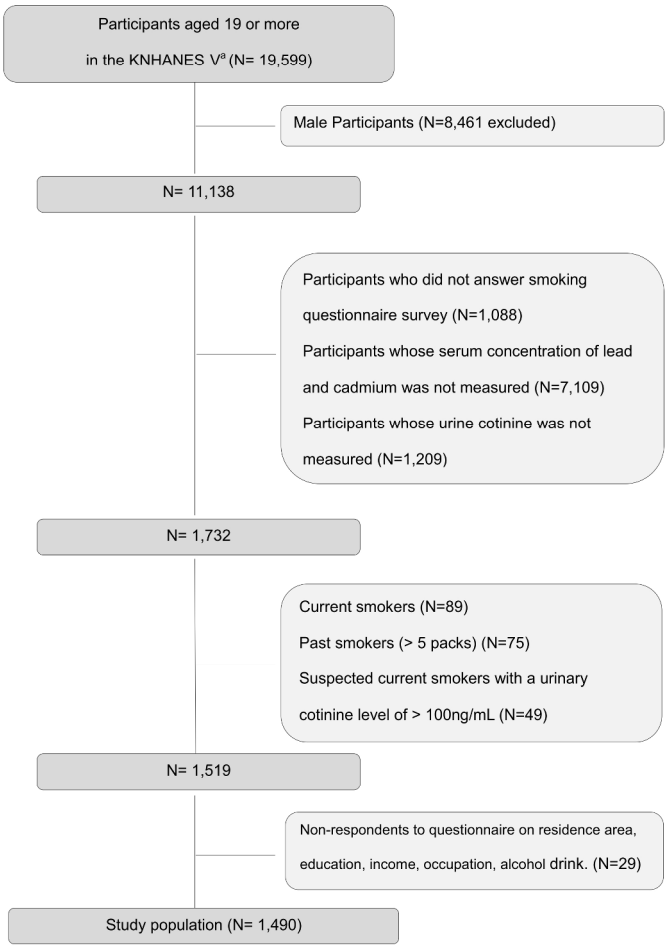
research : official journal of the Society for Research on Nicotine and Tobacco 2013;**15**(9):1608-16.

18. Lee B, Ha J. The effects of smoking and drinking on blood lead and cadmium levels: data from the fourth Korea national health and nutrition examination survey. Occupational and Environmental Medicine 2011;**68**(Suppl 1):A93-A93.
19. Shin J-Y, Kim J-M, Kim Y. The association of heavy metals in blood, fish consumption frequency, and risk of cardiovascular diseases among Korean adults: The Korean National Health and Nutrition Examination Survey (2008-2010). Korean J Nutr 2012;**45**(4):347-61.
20. Ashraf MW. Levels of Heavy Metals in Popular Cigarette Brands and Exposure to These Metals via Smoking. The Scientific World Journal 2012;**2012**:729430.
21. Shaham J, Meltzer A, Ashkenazi R, et al. Biological monitoring of exposure to cadmium, a human carcinogen, as a result of active and passive smoking. Journal of occupational and environmental medicine / American College of Occupational and Environmental Medicine 1996;**38**(12):1220-8.
22. Willers S, Gerhardsson L, Lundh T. Environmental tobacco smoke (ETS) exposure in children with asthma—relation between lead and cadmium, and cotinine concentrations in urine. Respiratory Medicine 2005;**99**(12):1521-27.
23. Apostolou A, Garcia-Esquinas E, Fadrowski JJ, et al. Secondhand tobacco smoke: a source of lead exposure in US children and adolescents. American journal of public health 2012;**102**(4):714-22.
24. Richter PA, Bishop EE, Wang J, et al. Trends in tobacco smoke exposure and blood lead levels among youths and adults in the United States: the National Health and Nutrition Examination Survey, 1999-2008. Preventing chronic disease 2013;**10**:E213.
25. Nordberg GF, Fowler BA, Nordberg M, et al. *Handbook on the Toxicology of Metals*: Academic Press, 2011.
26. Kim SH. Investigation of food metals in food and risk asseement in S.Korea. Secondary Investigation of food metals in food and risk asseement in S.Korea 2011. http://m.mfds.go.kr/jsp/livinginfo_v.jsp?site_code=1&board_code=31&seq=16682&page=31&searchText=.
27. Roh SJ. Concentration of blood heavy metal monitoring in the fifth Korea National Health and Nutrition Examination Survey(KNHANES, 2010). Secondary Concentration of blood heavy metal monitoring in the fifth Korea National Health and Nutrition Examination Survey(KNHANES, 2010) 2010.
28. Kim KH, Lee CM, Park SM, et al. Secondhand smoke exposure and osteoporosis in never-smoking postmenopausal women: the Fourth Korea National Health and Nutrition Examination Survey. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 2013;**24**(2):523-32.
29. Seo HG. ITC Korea National Report Waves 1 to 3 (2005-2010). Secondary ITC Korea National

Report Waves 1 to 3 (2005-2010) 2012. http://www.itcproject.org/resources/view/1139.

30. Ayers JW, Hofstetter CR, Hughes SC, et al. Smoking on both sides of the pacific: home smoking restrictions and secondhand smoke exposure among Korean adults and children in Seoul and California. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 2010;**12**(11):1142-50.

Figure 1. Study population




210x297mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract : page 2 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found : page 2 |
| **Introduction** | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported : pages 3-4 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses : page 4 |
| **Methods** | | |
| Study design | 4 | Present key elements of study design early in the paper: pages 4-6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection : pages 4-5 |
| Participants | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed<br>*Case-control study*—For matched studies, give matching criteria and the number of controls per case: pages 4-5 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable : pages 4-7 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group : pages 4-6 |
| Bias | 9 | Describe any efforts to address potential sources of bias: page 15 |
| Study size | 10 | Explain how the study size was arrived at: page 4 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why: page 7 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding: page 7 |
| | | (*b*) Describe any methods used to examine subgroups and interactions: page 7 |
| | | (*c*) Explain how missing data were addressed: page 7 |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed<br>*Case-control study*—If applicable, explain how matching of cases and controls was addressed<br>*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy: page 7 |
| | | (*e*) Describe any sensitivity analyses |

Continued on next page

| | | |
|---|---|---|
| **Results** | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed: pages 7-12 |
| | | (b) Give reasons for non-participation at each stage: pages 7-12 |
| | | (c) Consider use of a flow diagram: pages 7-12 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders: pages 7-12 |
| | | (b) Indicate number of participants with missing data for each variable of interest: pages 7-12 |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) : pages 7-12 |
| Outcome data | 15* | *Cohort study*—Report numbers of outcome events or summary measures over time |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures: pages 7-12 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included: pages 7-12 |
| | | (*b*) Report category boundaries when continuous variables were categorized: pages 7-12 |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |
| **Discussion** | | |
| Key results | 18 | Summarise key results with reference to study objectives: pages 12-16 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias: pages 12-16 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence: pages 12-16 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results: pages 12-16 |
| **Other information** | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based: page 16 |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.