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Original Article

Fraction of Cancer Attributable to Occupational Carcinogens in Korea between 2015 and 2030

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Purpose This study aimed to estimate the contribution of occupational carcinogens to cancer incidence and mortality in the Korean population between 2015 and 2030.

Materials and Methods We selected occupational carcinogens classified as International Agency for Research on Cancer (IARC) group 1 and estimated the prevalence of exposure using data from the Korean CARcinogen EXposure (K-CAREX) and previous studies. Relative risks were calculated using published literature through a meta-analysis. Levin's formula was used to estimate population attributable fraction (PAF) while considering a 15-year latency period between exposure, cancer incidence, and death. Additionally, trends in cancer PAF were calculated up to 2030, assuming constant relative risks and a 15-year latency period.

Results In 2015, the PAFs for occupational carcinogen–related cancer incidence and mortality were 1.00% (men, 1.75%; women, 0.15%) and 1.97% (men, 2.98%; women, 0.33%), respectively, with asbestos being the largest contributor (incidence, 0.48%; mortality, 0.98%). In 2030, the PAFs for occupational carcinogen-related cancer incidence and mortality were 0.34% (men, 0.62%; women, 0.07%) and 0.80% (men, 1.22%; women, 0.15%), respectively, with diesel engine exhaust being projected to become the largest contributor by 2030 (incidence, 0.16%; mortality, 0.39%).

Conclusion The PAFs of occupational carcinogens in Korea between 2015 and 2030 were estimated to be very low in the general population, and the values are expected to decrease over time owing to various regulations to prevent exposure to occupational carcinogens. Therefore, while regulating well-known occupational carcinogens, efforts should be made to monitor newly identified ones to ensure prompt implementation of preventive measures.

Key words Population attributable fraction, Attributable count, Occupational carcinogens, K-CAREX

Introduction

The concept of population attributable fraction (PAF) originated from the calculation of the attributable fraction of lung cancer caused by smoking in the U.S. population in 1981 [1]. Removing occupational carcinogens may allow for an estimation of preventable cancer incidence and associated mortality. PAF is widely used as an important tool to guide public health policies for diseases [2].

According to the International Agency for Research on Cancer (IARC) [3], occupational environments could be exposed to 47 of 129 carcinogens classified as definitely carcinogenic to humans (group 1) [4,5]. In addition to the risk of breast cancer associated with night-shift work, there is evidence of exposure-related risks of prostate cancer and colorectal cancer [6]. This suggests that the disease burden from exposure to occupational factors may remain a significant issue.

Effective control or elimination of exposure to occupational factors can play an important role in cancer prevention because they tend to affect a definite target group by legislation [7]. Asbestos is a representative occupational carcinogen that was first banned in Denmark in 1986 and in Korea in 2009 [8,9]. Subsequently, the Industrial Accident Compensation Insurance Act (IACI Act) was amended in July 2013 to expand the scope of occupational cancer recognition. Furthermore, the Occupational Safety and Health Act was revised in October 2022 to incorporate eight additional occupationally hazardous substances and specially controlled substances to address emerging risks.

In 2021, Korea for the first time in Asia developed a carcinogen exposure estimation tool (Korean CARcinogen EXposure, K-CAREX) [10]. The CARcinogen EXposure (CAREX) program, which was developed in Canada [11], remains the most commonly used method for estimating the prevalence of occupational carcinogen exposure. This tool enables the

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estimation of the number of people exposed to carcinogens in Korea's industrial environment. Korea has undergone rapid industrialization in a short period of time [12]. Therefore, it is imperative to assess the burden of cancer attributable to occupational factors according to the specific characteristics of Korea.

We aimed to estimate the degree of cancer prevention attributable to occupational exposure to carcinogens by calculating the PAF for cancer incidence and mortality between 2015 and 2030. This estimation accounts for a 15-year latency period between exposure to occupational carcinogens, as assessed by K-CAREX, and subsequent cancer incidence and mortality.

Materials and Methods

1. Identification of occupational carcinogens and target cancers

Among the carcinogens classified as group 1 by the IARC [5], 47 occupational carcinogens reported by Loomis et al. [4] were reviewed. Among them, substances for which occupational exposure was possible in Korea and data were available to estimate exposure prevalence in 2000 were selected.

For example, in the case of mineral oil, the risk was confirmed before industrialization and use of refined substances in Korea [13]. For beryllium, the number of exposed workers calculated using the K-CAREX was less than 10 because of the small number of exposed people in Korea [10]. In addition, prevalence of exposure could not be evaluated for pentachlorophenol, which was only included as a work environment carcinogen in 2020 under Article 125 of the IACI Act, and 12 of the IARC group 1 carcinogens, which were not subject to occupational assessment in Korea.

After excluding these substances, 10 occupational carcinogens were selected (S1 Table), and eight cancer types were targeted, including those with sufficient evidence in humans [5].

2. Estimation of relative risks for cancer

A meta-analysis of literature published between 1990 and April 2020 was conducted to determine the relative risks (RR) of cancers associated with occupational carcinogens, utilizing both the PubMed (MEDLINE) and Embase databases. We included global studies and systematic reviewed those that met the PICOTS-SD criteria, owing to the limited number of studies on cancer incidence and deaths associated with occupational carcinogens (S2 Table). To improve the accuracy of summary RR, we prioritized the inclusion of studies where the occupational exposure of the study population was clear, or where the time of entry into the company (time of exposure) was considered, or where exposure levels were calculated separately, or where values corrected for multiple exposure factors were reported. In the primary inclusion criteria, studies conducted among a Korean or Asian cohort and case-control studies were selected. In the case of global case-control studies, only those lacking sufficient literature were deemed eligible for inclusion. Summary RR were calculated without stratification by sex or outcome variables (such as incidence and mortality) because of the small number of studies, except for ovarian and prostate cancers, for which stratification by sex was applied. For the sensitivity analysis, we conducted a meta-analysis using a systematic review of global studies on the association between occupational carcinogens and cancer risk. Statistical analyses of the summary RR and 95% confidence intervals were conducted using random-effects models. All statistical analyses were performed using R Software ver. 3.6.4 (R Foundation for Statistical Computing).

3. The proportion of workers exposed to individual carcinogens

The number of workers exposed to most occupational carcinogens was calculated using the K-CAREX and substituted into the population census data by industry, sex, and year [10]. For industries that underwent changes during this period, the number of exposed workers following consolidation or separation was calculated using a linkage table. As the development of the K-CAREX was based on data from 2010, the third-quartile (Q3) value of the judgment of experts was utilized to estimate the number of workers exposed to occupational carcinogens between 2000 and 2005, and the median value of the judgment of experts was employed to estimate the number of exposed workers between 2010 and 2015 [14]. The exception was asbestos, which has been banned since 2009. The number of workers from 2000 to 2005 was calculated based on experts' estimates by industry from the 1995 National Enterprise Survey [15]. For diesel engine exhaust, which was not included in the K-CAREX, the number of exposed workers between 2005 and 2015 was calculated by applying industry-specific fractions calculated based on the 1993 European CAREX used in the study by Park et al. [16]. Finally, to reflect past exposure, the number of exposed workers was calculated by imputing the turnover rates of men and women (4.3 and 4.1, respectively) surveyed by the National Employment Information Service [17]. Data from the Korean Population and Housing Census for adults aged 20 years and older served as the denominator to estimate the prevalence of exposure by occupational factor and sex between 2000 and 2015.

4. Calculation of occupational carcinogen–related cancer PAF

Cancer PAFs for occupational carcinogens, cancer sites, and sex were calculated by substituting the prevalence of exposure (P_e) and summary RR using Levin's formula [18].

$$PAF=\frac{\sum P_e(RR-1)}{\sum P_e(RR-1)+1} \quad (1)$$

If the summary RRs of occupational carcinogens and cancer sites were less than 1, they were excluded from PAF estimation. To calculate attributed cases (AC) among adults aged 20 years and older in 2015, data on the number of cancer cases and deaths were obtained from the National Cancer Registration Statistics of the Central Cancer Registry at the National Cancer Center and the Cause of Death Statistics of Statistics Korea [19,20]. AC, representing the number of attributable cancer cases or deaths, were calculated as the value of PAF (%) for all occupational carcinogens, cancer sites, and sex categories. Total AC was calculated by adding all ACs for occupational carcinogens, cancer sites, and sex. Total cancer PAF (%) was calculated by dividing the sum of the total AC by the total number of cancer cases or deaths. A sensitivity analysis was conducted to assess the difference in PAF among occupational carcinogens using summary RR from global studies.

5. PAF projection

To calculate changes and trends in cancer PAF between 2015 and 2030, we assumed a 15-year latency period. Throughout this period, the RR remained constant, and the exposure prevalence rates between 2005 and 2015, calculated as previously described, were utilized.

The projected populations for 2025 and 2030, along with the projected number of cancer cases and deaths, were obtained from previous literature [21]. The methodology employed for forecasting these estimates entailed calculating the average annual percentage change (AAPC) in standardized cancer incidence and mortality rate by age and sex for each cancer type, using a joinpoint regression model.

Joinpoint regression (x=year, Y= Ln[rate]) was calculated as follows:

$$\log(Y)=\beta 0-\beta 1X \quad (2)$$

AAPC was calculated as follows:

$$AAPC=(e^{\beta 1}-1)\times 100 \quad (3)$$

The methodology has been described in detail in previous literature [21].

The total population for 2025 and 2030 was estimated using age-sex population trend data from the National Statistics Office of Korea, and the expected numbers of cases and deaths were calculated as follows:

$$I_d=\sum_{j=x}^{y} IR_{2000,\,j}\times N_{2020,\,j} \quad (4)$$

$$D_d=\sum_{j=x}^{y} DR_{2000,\,j}\times N_{2020,\,j} \quad (5)$$

where incidence rate (*IR*) and death rate (*DR*) represent the incidence and death rates, respectively, and *N* denotes the population size.

Results

1. RRs of cancer

Summary RRs derived from Korean cohort studies were identified for three occupational carcinogens-cancer sites pairs: benzene-leukemia (Korea-RR, 1.81), crystalline silica dust-lung cancer (Korea-RR, 1.38) [22,23], and chromium-lung cancer (Korea-RR, 0.93; Asia-RR, 1.09) (Table 1). The RR for formaldehyde-nasopharynx cancer (1.30) was derived from only one case-control study in Asia (population-based 2, hospital-based 1). Asbestos-mesothelioma (Asia-RR, 44.56) had the highest RR among the eight cancer sites, followed by nickel-sinonasal cancer (Asia-RR, 18.15) and asbestos-lung cancer (Asia-RR, 3.23).

The sensitivity analysis using meta-analyzed RRs in global studies showed significantly high values in the same order. However, Global-RR (14.36) of asbestos-mesothelioma was significantly lower than Asia-RR. The meta-analyzed RRs in Asian studies were higher than those in global studies, except for chromium-lung cancer, formaldehyde-nasopharynx cancer, and asbestos-ovarian cancer (S3-S17 Tables). Except for asbestos-mesothelioma and lung cancer, the summary RRs for both global and Asian studies were below 2.00.

2. Prevalence of exposure

In the year 2000, the prevalence of exposure to 10 occupational carcinogens was 12.91% (21.86% in men and 4.24% in women). Diesel engine exhaust had the highest prevalence among the 10 occupational carcinogens, affecting both men and women. For men, this was followed by nickel (3.82%), crystalline silica dust (2.72%), and asbestos (2.34%), with the prevalence of other carcinogens being < 2%. For women, this was followed by formaldehyde (0.91%) and nickel (0.56%), with the prevalence of other factors except diesel engine exhaust being < 1% (Table 2).

The prevalence of exposure decreased significantly until 2015 (men, 13.43%; women, 3.04%), with a greater decline

Table 1. RRs for exposure to occupational carcinogens

Occupational factors	Cancers	This study[a]			Global study[b] (all studies)	
		Country	Study (CCS)	RR (95% CI)	Study (CCS)	RR (95% CI)
Asbestos	Larynx (C32)	Asia	2	1.82 (0.35-9.35)	25	1.52 (1.30-1.79)
	Lung (C33-C34)	Asia	10	3.23 (2.52-4.13)	44	2.14 (1.88-2.44)
	Mesothelioma (C45)	Asia	3	44.56 (11.95-166.09)	27	14.36 (9.94-20.76)
	Ovary (C56)	Asia+Global	19	1.79 (1.40-2.30)	19	1.79 (1.40-2.30)
Silica dust, crystalline	Lung (C33-C34)	Korea	2	1.38 (0.97-1.96)	49	1.44 (1.33-1.56)
Diesel engine exhaust	Lung (C33-C34)	Global	18	1.23 (1.15-1.32)	18	1.23 (1.15-1.32)
Benzene	Leukemia (C91-C95)	Korea	2	1.81 (0.99-3.31)	19	1.49 (1.28-1.74)
Nickel compounds	Sinonasal (C30-C31)	Global	5	18.15 (14.27-23.09)	5	18.15 (14.27-23.09)
	Lung (C33-C34)	Global	15	1.50 (1.29-1.76)	15	1.50 (1.29-1.76)
Chromium (VI)	Lung (C33-C34)	Korea+Asia	3	1.09 (0.78-1.54)	34	1.25 (1.14-1.38)
Cadmium	Lung (C33-C34)	Global	5	1.18 (0.97-1.42)	5	1.18 (0.97-1.42)
1,3-Butadiene	Leukemia (C91-C95)	Global	5	1.37 (1.04-1.79)	5	1.37 (1.04-1.79)
Formaldehyde	Leukemia (C91-C95)	Global	8	1.04 (0.92-1.17)	8	1.04 (0.92-1.17)
	Nasopharynx (C11)	Asia	3 (3)	1.30 (0.81-2.10)	8 (3)	1.51 (0.97-2.36)
Trichloroethylene	Kidney (C64)	Global	12	1.34 (1.00-1.81)	12	1.34 (1.00-1.81)

Exposure vs. non-exposure (reference). Relative risk (RR) was meta-analyzed using all estimates, including the hazard ratio, odds ratio, standardized incidence rate ratio, standardized incidence ratio, and standardized mortality ratio. CI, confidence interval; CCS, case-control study. [a]The RR is calculated by substituting the value of Korean study priorities, [b]The RR is calculated by substituting the value of the all studies.

observed among men compared with women. The prevalence of exposure to asbestos, which was banned in 2009, was calculated using the K-CAREX to be 0.06% in 2015. Between 2010 and 2015, the smallest prevalence change was observed for cadmium in both sexes, whereas an increase was observed for 1,3-butadiene exposure. Exposure to the remaining substances decreased in men but increased in women.

3. PAF of cancer

Among Korean adults aged 20 years and older in 2015, occupational carcinogens contributed to 2,150 cancer cases (1.00%) and 1,512 cancer deaths (1.97%) (Table 3, Figs. 1A and 2A). The fraction caused by occupational carcinogens was higher in men than in women (1.75% vs. 0.15% of cancer cases and 2.98% vs. 0.33% of cancer deaths) (Table 3, Figs. 1B and C, 2B and C). Asbestos was the largest contributor to occupational cancer (incidence, 0.48%; mortality, 0.98%), followed by diesel engine exhaust (incidence, 0.20%; mortality, 0.40%) and nickel (incidence, 0.21%; mortality, 0.38%). The asbestos exposure–related risk of cancer, except for laryngeal cancer, was significantly high.

The sensitivity analysis using global RR showed that the cancer PAF for occupational carcinogens was lower than the results obtained by prioritizing the substitution of Asia-RR of cancer cases (global PAF: 0.79% for total, 1.39% for men, and 0.12% for women) and cancer deaths (global PAF: 1.55% for total, 2.34% for men, and 0.26% for women) (Table 3). The overall ranking of the PAFs calculated by occupational carcinogen remained unchanged.

Incidence of cancer attributed to exposure to formaldehyde and 1,3-butadiene yielded results indicating fewer than 10 cases, with an overall cancer PAF approaching 0% (S18 Table). Lung cancer constituted 89.66% of all cancer cases and 92.91% of cancer-related deaths attributable to occupational carcinogens (Figs. 1A and 2A), followed by sinonasal cancer (cases, 5.30%; deaths, 2.78%) and mesothelioma (cases, 2.47%; deaths, 2.98%).

4. PAF projection

The total number of cases and deaths attributable to occupational carcinogens will be halved in 2030 compared with 2015, with occupational carcinogens contributing to 1,237 cancer cases (0.34%) and 749 cancer deaths (0.80%) in 2030 (Table 4, Figs. 3A and 4A). Following a substantial decline, the proportion of occupational carcinogens attributable to cancer exhibited a modest increase in 2030 compared with 2025, particularly among women (2025 and 2030, respectively: incidence PAFs 0.06% and 0.07%; death PAFs 0.12% and 0.15%) (Table 4, Figs. 3B and C, 4B and C). In 2030, diesel engine exhaust was identified as the primary occupational carcinogen, with an incidence PAF of 0.16% and a death PAF of 0.39%.

Incidences of cancer attributed to exposures to asbestos, nickel, and trichloroethylene were more than 10 cases. Lung

Table 2. Prevalence (%) of exposure to occupational carcinogens in Korea

	2000[a]	2005[a]	2010[b]	2015[b]
Occupational carcinogen				
Men	21.86	17.13	13.96	13.43
Women	4.24	3.65	2.60	3.04
Total	12.91	10.30	8.15	8.21
Asbestos				
Men	2.45[c]	2.53[c]	0.10	0.10
Women	0.34[c]	0.34[c]	0.01	0.02
Total	1.38[c]	1.42[c]	0.06	0.06
Silica dust, crystalline				
Men	2.72	1.18	1.20	1.14
Women	0.36	0.16	0.17	0.19
Total	1.52	0.66	0.67	0.66
Diesel engine exhaust[d]				
Men	10.00	10.06	9.15	8.67
Women	2.28	2.39	1.82	2.18
Total	6.08	6.19	5.40	5.41
Benzene				
Men	0.81	0.34	0.35	0.37
Women	0.16	0.05	0.06	0.07
Total	0.48	0.19	0.20	0.22
Nickel compounds				
Men	3.82	2.01	2.25	2.23
Women	0.56	0.28	0.32	0.36
Total	2.17	1.13	1.26	1.29
Chromium(VI) compounds				
Men	0.65	0.25	0.27	0.27
Women	0.14	0.05	0.05	0.06
Total	0.39	0.15	0.16	0.16
Cadmium and cadmium compounds				
Men	0.26	0.09	0.10	0.10
Women	0.06	0.02	0.02	0.02
Total	0.16	0.05	0.06	0.06
1,3-Butadiene				
Men	0.18	0.07	0.07	0.08
Women	0.03	0.01	0.01	0.02
Total	0.10	0.04	0.04	0.05
Formaldehyde				
Men	1.26	0.54	0.53	0.56
Women	0.91	0.41	0.51	0.61
Total	1.08	0.47	0.52	0.59
Trichloroethylene				
Men	0.96	0.60	0.48	0.48
Women	0.31	0.36	0.13	0.14
Total	0.63	0.47	0.30	0.31

[a]Third quartile (Q3) value of expert estimates using the Korean CARcinogen EXposure (K-CAREX) [10], [b]The median value of expert estimates using the K-CAREX [10], [c]The values of expert estimates [15], [d]The values of expert estimates using the CARcinogen EXposure (CAREX) [16].

Table 3. PAF (%) of occupational carcinogen–related cancer by RR in 2015

	PAF (%) using RR for Korean study priorities						PAF (%) using RR of global study					
	Total		Men		Women		Total		Men		Women	
	PAF (%)	AC	PAF (%)	AC	PAF (%)	AC	PAF (%)	AC	PAF (%)	AC	PAF (%)	AC
Incidence												
Asbestos	0.48	1,031	0.85	962	0.07	69	0.25	542	0.85	504	0.04	38
Silica dust, crystalline	0.09	186	0.15	176	0.01	10	0.10	252	0.15	203	0.01	12
Diesel engine exhaust	0.20	426	0.34	388	0.04	38	0.20	426	0.34	388	0.04	38
Benzene	0.01	12	0.01	10	0.00	2	0.00	7	0.01	6	0.00	1
Nickel compounds	0.21	459	0.38	428	0.03	31	0.21	459	0.38	428	0.03	31
Chromium(VI) compounds	0.01	11	0.01	10	0.00	1	0.01	30	0.01	9	0.00	2
Cadmium and its compounds	0.00	10	0.01	9	0.00	1	0.00	10	0.01	9	0.00	1
1,3-Butadiene	0.00	1	0.00	1	0.00	0	0.00	1	0.00	1	0.00	0
Formaldehyde	0.00	3	0.00	2	0.00	1	0.00	3	0.00	3	0.00	0
Trichloroethylene	0.01	12	0.01	10	0.00	2	0.01	12	0.01	10	0.00	2
All cancers (95% CI)	1.00	2,150	1.75	1,996	0.15	154	0.79	1,705	1.39	1,580	0.12	125
Lower	0.59	1,261	1.03	1,173	0.09	88	0.54	1,172	0.96	1,090	0.08	82
Upper	1.60	3,438	2.81	3,191	0.24	247	1.07	2,304	1.87	2,129	0.17	175
Death												
Asbestos	0.98	748	1.48	704	0.15	44	0.81	391	0.77	368	0.08	23
Silica dust, crystalline	0.18	136	0.27	129	0.02	7	0.21	158	0.32	150	0.03	8
Diesel engine exhaust	0.40	310	0.60	285	0.09	25	0.40	310	0.60	285	0.09	25
Benzene	0.01	7	0.01	6	0.00	1	0.01	5	0.01	4	0.00	1
Nickel compounds	0.38	293	0.58	275	0.06	18	0.38	293	0.58	275	0.06	18
Chromium(VI) compounds	0.01	8	0.02	8	0.00	0	0.03	21	0.04	20	0.00	1
Cadmium and its compounds	0.01	6	0.01	6	0.00	0	0.01	6	0.01	6	0.00	0
1,3-Butadiene	0.00	1	0.00	1	0.00	0	0.00	1	0.00	1	0.00	0
Formaldehyde	0.00	1	0.00	1	0.00	0	0.00	1	0.00	1	0.00	0
Trichloroethylene	0.00	2	0.00	2	0.00	0	0.00	2	0.00	2	0.00	0
All cancers (95% CI)	1.97	1,512	2.98	1,417	0.33	95	1.55	1,188	2.34	1,112	0.26	76
Lower	1.16	887	1.75	832	0.19	55	1.07	817	1.61	766	0.18	51
Upper	3.09	2,365	4.65	2,211	0.53	154	2.09	1,604	3.15	1,499	0.36	105

AC, attributable count; CI, confidence interval; PAF, population attributable fraction; RR, relative risk.

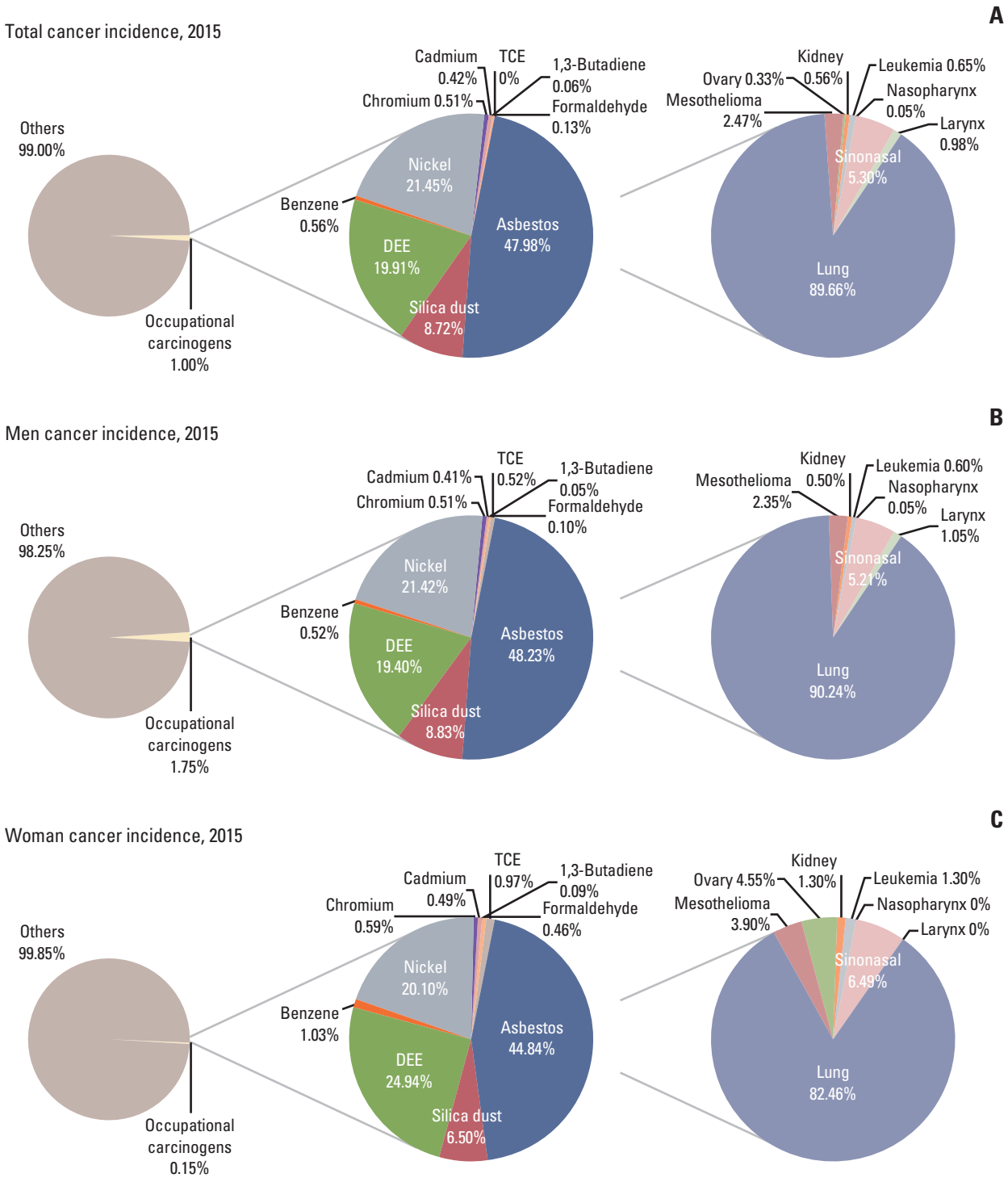

Fig. 1. The proportion of specific cancers incidence among all cancers attributable to occupational carcinogens, and the proportion by carcinogen, in 2015. (A) Total cancer incidence, 2015. (B) Men cancer incidence, 2015. (C) Woman cancer incidence, 2015. DEE, diesel engine exhaust; TCE, trichloroethylene.

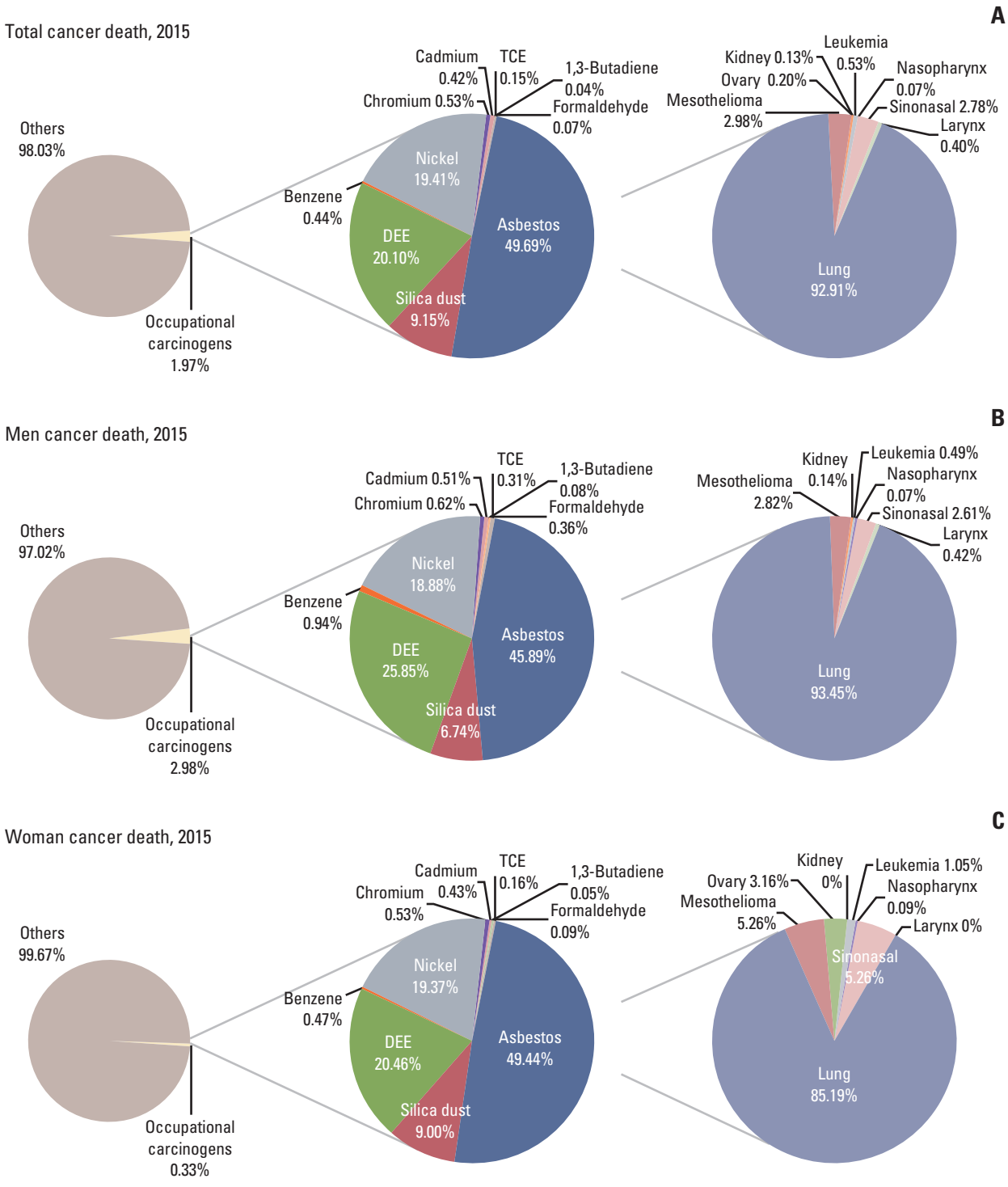

Fig. 2. The proportion of specific cancers death among all cancers attributable to occupational carcinogens, and the proportion by carcinogen, in 2015. (A) Total cancer death, 2015. (B) Men cancer death, 2015. (C) Woman cancer death, 2015. DEE, diesel engine exhaust; TCE, trichloroethylene.

Table 4. PAF (%) of occupational carcinogen–related cancer between 2015 and 2030

	Total								Men								Women							
	2015		2020		2025		2030		2015		2020		2025		2030		2015		2020		2025		2030	
	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC
Incidence																								
By carcinogen																								
Asbestos	0.48	1,031	0.49	1,215	0.02	61	0.02	72	0.85	962	0.87	1,129	0.04	58	0.04	67	0.07	69	0.07	86	0.00	3	0.00	5
Silica	0.09	186	0.04	94	0.04	112	0.03	123	0.15	176	0.07	88	0.07	104	0.06	113	0.01	10	0.00	6	0.01	8	0.01	10
DEE	0.20	426	0.20	495	0.17	524	0.16	584	0.34	388	0.34	445	0.31	475	0.28	513	0.04	38	0.04	51	0.03	49	0.04	71
Benzene	0.01	12	0.00	6	0.00	7	0.00	9	0.01	10	0.00	5	0.00	6	0.00	8	0.00	2	0.00	1	0.00	1	0.00	1
Nickel	0.21	459	0.11	283	0.12	368	0.12	421	0.38	428	0.20	263	0.22	341	0.20	385	0.03	31	0.02	19	0.02	27	0.02	36
Chromium	0.01	11	0.00	4	0.00	5	0.00	6	0.01	10	0.00	4	0.00	5	0.00	5	0.00	1	0.00	0	0.00	0	0.00	1
Cadmium	0.00	10	0.00	4	0.00	5	0.00	5	0.01	9	0.00	4	0.00	5	0.00	5	0.00	1	0.00	0	0.00	0	0.00	0
1,3-Butadiene	0.00	1	0.00	0	0.00	0	0.00	1	0.00	1	0.00	0	0.00	0	0.00	1	0.00	0	0.00	0	0.00	0	0.00	0
Formaldehyde	0.00	3	0.00	1	0.00	1	0.00	2	0.00	2	0.00	1	0.00	1	0.00	2	0.00	0	0.00	0	0.00	0	0.00	0
TCE	0.01	12	0.00	10	0.00	10	0.00	14	0.01	10	0.01	8	0.01	9	0.01	12	0.00	2	0.00	2	0.00	1	0.00	2
By cancer type																								
Nasopharynx	0.24	1	0.24	1	0.24	1	0.24	1	0.38	1	0.16	1	0.16	1	0.17	1	0.27	0	0.12	0	0.15	0	0.18	0
Sinonasal	29.84	114	18.48	73	20.35	93	20.46	106	39.61	104	25.66	67	27.81	85	27.66	96	8.77	10	4.61	6	5.23	8	5.77	10
Larynx	1.82	21	1.91	23	0.08	1	0.09	1	1.97	21	2.04	23	0.08	1	0.08	1	0.28	0	0.28	0	0.01	0	0.01	0
Lung	7.84	1,928	6.67	1,929	2.84	975	2.70	1,095	10.46	1,801	9.10	1,788	3.89	896	3.74	983	1.72	127	1.52	141	0.68	79	0.79	112
Mesothelioma	38.13	53	38.75	62	2.74	6	3.14	9	51.66	47	52.48	55	4.13	6	4.13	8	13.05	6	13.00	7	0.64	0	0.64	1
Ovary	0.27	7	0.27	8	0.01	0	0.01	0	-	0	0.00	0	0.00	0	0.00	0	0.27	7	0.27	8	0.01	0	0.01	0
Kidney	0.26	12	0.17	10	0.12	10	0.13	14	0.33	10	0.20	8	0.16	9	0.16	12	0.11	2	0.12	2	0.05	1	0.05	2
Leukemia	0.49	14	0.19	6	0.18	7	0.24	11	0.75	12	0.27	5	0.27	6	0.38	10	0.14	2	0.07	1	0.06	1	0.05	1
All cancers	1.00	2,150	0.86	2,112	0.36	1,093	0.34	1,237	1.75	1,996	1.50	1,947	0.63	1,004	0.62	1,111	0.15	154	0.14	165	0.06	89	0.07	126
Death																								
By carcinogen																								
Asbestos	0.98	748	1.02	838	0.05	42	0.05	50	1.48	704	1.56	792	0.07	40	0.08	47	0.15	44	0.15	46	0.01	2	0.01	3
Silica	0.18	136	0.08	65	0.08	74	0.08	77	0.27	129	0.12	62	0.13	70	0.13	73	0.02	7	0.01	3	0.01	4	0.01	4
DEE	0.40	310	0.41	339	0.39	343	0.39	363	0.60	285	0.62	312	0.59	320	0.58	333	0.09	25	0.09	27	0.07	23	0.08	30
Benzene	0.01	7	0.00	3	0.00	3	0.01	5	0.01	6	0.01	3	0.01	3	0.01	4	0.00	1	0.00	0	0.00	0	0.00	1
Nickel	0.38	293	0.22	177	0.25	221	0.26	245	0.58	275	0.33	168	0.38	209	0.40	230	0.06	18	0.03	9	0.04	12	0.04	15
Chromium	0.01	8	0.00	3	0.00	3	0.00	4	0.02	8	0.01	3	0.01	3	0.01	3	0.00	0	0.00	0	0.00	0	0.00	1
Cadmium	0.01	6	0.00	3	0.00	3	0.00	3	0.01	6	0.00	3	0.01	3	0.01	3	0.00	0	0.00	0	0.00	0	0.00	0
1,3-Butadiene	0.00	1	0.00	0	0.00	0	0.00	0	0.00	1	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0
Formaldehyde	0.00	1	0.00	0	0.00	0	0.00	0	0.00	1	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0
TCE	0.00	2	0.00	2	0.00	1	0.00	2	0.00	2	0.00	2	0.00	1	0.00	2	0.00	0	0.00	0	0.00	0	0.00	0

(Continued to the next page)

Table 4. Continued

	Total								Men								Women							
	2015		2020		2025		2030		2015		2020		2025		2030		2015		2020		2025		2030	
	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC	PAF	AC
By cancer type																								
Nasopharynx	0.60	1	0.15	0	0.00	0	0.00	0	0.38	1	0.16	0	0.16	0	0.17	0	0.27	0	0.12	0	0.15	0	0.18	0
Sinonasal	28.19	42	19.16	32	20.10	40	20.09	46	39.61	37	25.66	30	27.81	37	27.66	42	8.77	5	4.61	2	5.23	3	5.77	4
Larynx	1.74	6	1.87	6	0.00	0	0.00	0	1.97	6	2.04	6	0.08	0	0.08	0	0.28	0	0.28	0	0.01	0	0.01	0
Lung	8.08	1,405	7.13	1,332	3.05	640	2.99	686	10.44	1,324	9.10	1,258	3.88	602	3.74	638	1.72	81	1.53	74	0.70	38	0.81	48
Mesothelioma	39.47	45	39.23	51	2.84	6	2.99	10	51.66	40	52.48	46	4.13	6	4.13	9	13.05	5	13.00	5	0.64	0	0.64	1
Ovary	0.27	3	0.27	4	0.01	0	0.01	0	-	0	0.00	0	0.00	0	0.00	0	0.27	3	0.27	4	0.01	0	0.01	0
Kidney	0.21	2	0.19	2	0.08	1	0.14	2	0.33	2	0.20	2	0.16	1	0.16	2	0.11	0	0.12	0	0.05	0	0.05	0
Leukemia	0.48	8	0.17	3	0.15	3	0.23	5	0.74	7	0.30	3	0.26	3	0.32	4	0.14	1	0.06	0	0.00	0	0.11	1
All cancers	1.97	1,512	1.74	1,430	0.78	690	0.80	749	2.98	1,417	2.65	1,345	1.19	649	1.22	695	0.33	95	0.27	85	0.12	41	0.15	54

AC, attributable count; DEE, diesel engine exhaust; PAF, population attributable fraction; TCE, trichloroethylene.

cancer constituted 88.52% of all cancer cases and 91.58% of cancer-related deaths attributable to occupational carcinogens (Figs. 3A and 4A). This was followed by sinonasal cancer (cases, 5.30%; deaths, 2.78%).

Discussion

Among Korean adults aged 20 years and older in 2015, occupational carcinogens accounted for 1.00% of cancer cases and 1.97% of cancer deaths (n=2,150 and n=1,512, respectively). Lung cancer accounts for approximately 90% of cancer cases and deaths attributed to occupational carcinogens, followed by sinonasal cancer and mesothelioma. The numbers of cancer cases and deaths attributed to occupational carcinogens in 2030 are projected to decrease by approximately half the numbers in 2015 (1,237 cancer cases and 749 cancer deaths). It is important to note that the persistent pattern of a significant proportion of occupational cancers, such as lung cancer, will remain consistent in 2030, with no downward trend after 2025.

In view of the paucity of available data on cancer risk attributable to occupational factors [24], we calculated PAFs using Levin's formula, which is the most frequently used method for estimating PAFs by imputing risks estimated from published literature when personal information is not available. The methodology is suitable for interpretation on a factor-cancer-species basis. The Levin's formula has been utilized to estimate AF for a variety of occupational factors in addition to the Global Burden of Disease. The inability of the Levin's formula to account for interaction effects in occupational factors with multiple exposures has been identified as a significant limitation, which could lead to biased results being estimated in either direction [25,26]. It is therefore imperative to be fully aware of the potential for bias, the level of bias, and the direction of bias due to the application of the Levin's formula, as has been reported by a number of authors. Consequently, the results of extant studies and the present study should be interpreted with caution.

The United Kingdom and Canada, two of the most advanced countries in occupational cancer burden studies, report levels between 3.8% and 4.2% between 2005 and 2015 [27-30], using methodologies similar to those employed in this study. The present study revealed a lower occupational cancer PAF, compared with other countries. A significant contributing factor to this difference was the exclusion of occupational factors such as exposures to ultraviolet radiation and sulfuric acid, which are subject to higher frequencies of exposure in other countries. In addition, the results may represent an underestimation of asbestos-related PAF in this study, as PAF was calculated using only occupational expo-

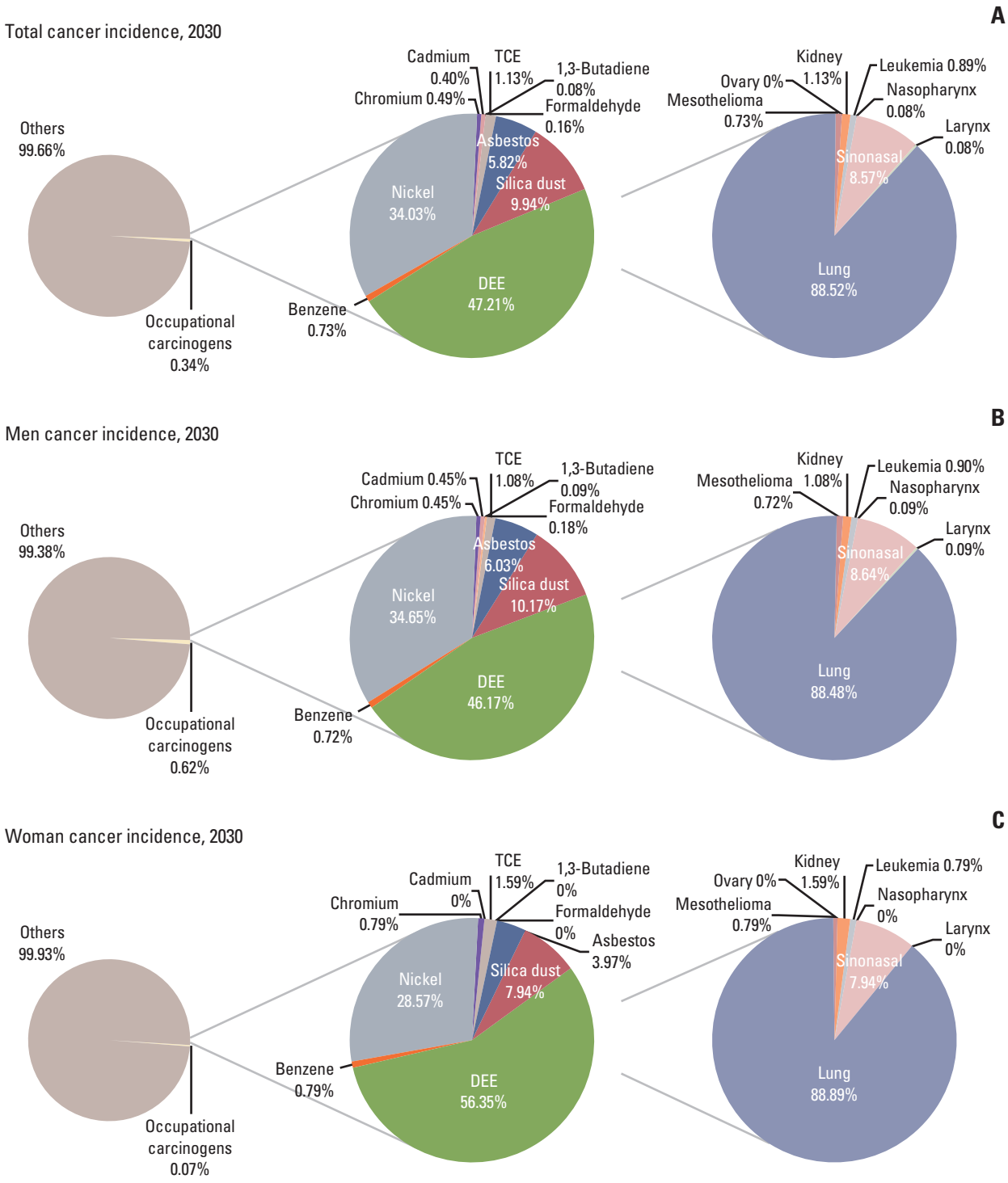

Fig. 3. The proportion of specific cancers incidence among all cancers attributable to occupational carcinogens, and the proportion by carcinogen, in 2030. (A) Total cancer incidence, 2030. (B) Men cancer incidence, 2030. (C) Woman cancer incidence, 2030. DEE, diesel engine exhaust; TCE, trichloroethylene.

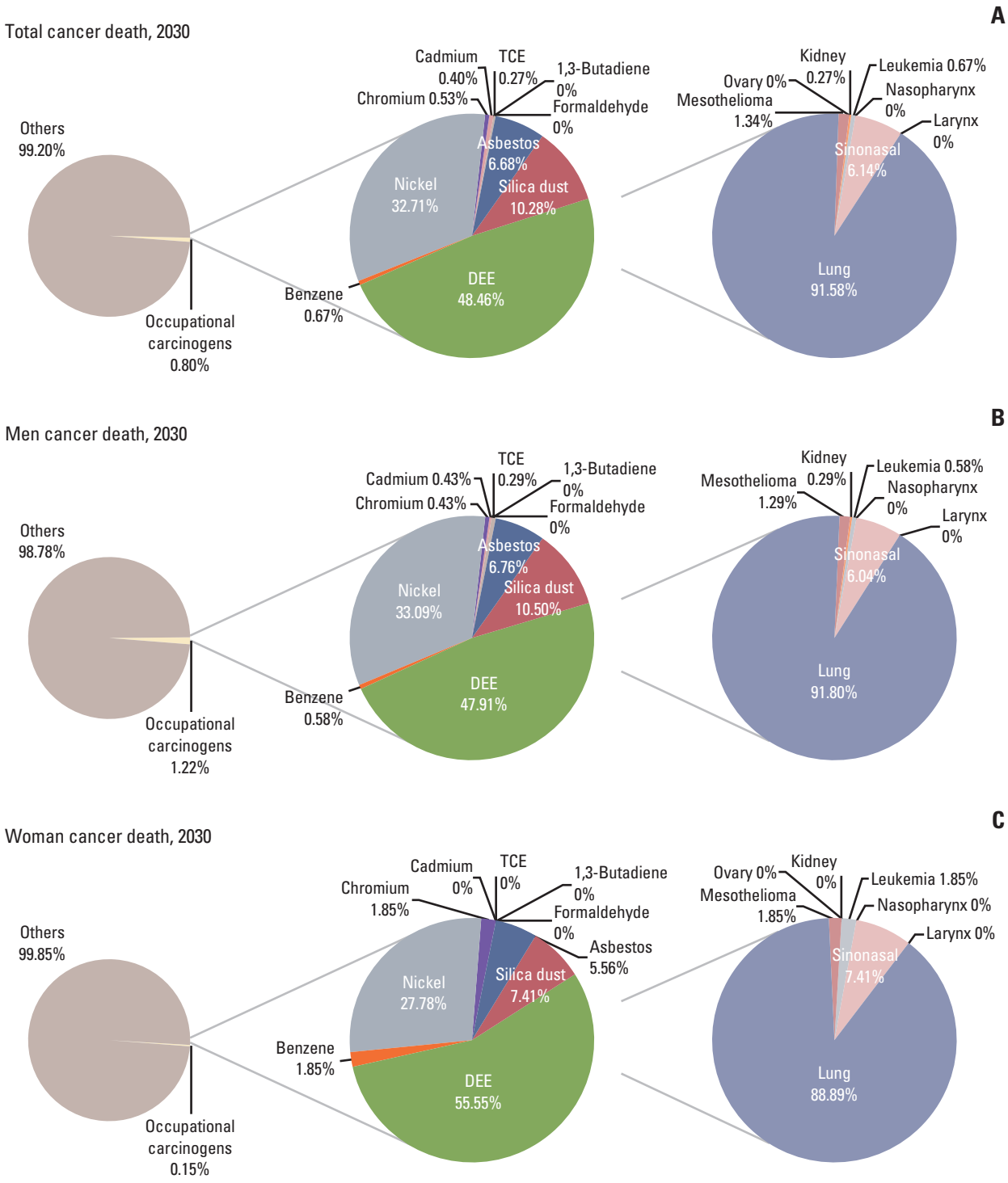

Fig. 4. The proportion of specific cancers death among all cancers attributable to occupational carcinogens, and the proportion by carcinogen, in 2030. (A) Total cancer death, 2030. (B) Men cancer death, 2030. (C) Woman cancer death, 2030. DEE, diesel engine exhaust; TCE, trichloroethylene.

sure rather than environmental exposure.

We calculated summary RRs from meta-analyses, incorporating literature from Korea along with global literature. Consequently, the results should be interpreted with caution, as they may be subject to bias resulting from risk imputation due to differences in exposure levels and timing in occupational settings between countries. When calculating the RRs, an effort was made to selectively incorporate literature published after 1990 to reflect the nearest time point. Furthermore, in order to enhance the precision of the estimates, a priority was assigned to the inclusion of results that had been calculated by separating exposure levels or where corrected values had been reported for multiple exposure factors (e.g., asbestos and smoking exposure adjusted values were selected for nickel-lung cancer calculations). Based on the sensitivity analysis results in this study, the summary RRs for Asian studies were higher than those for global studies (except for chromium-related lung cancer, formaldehyde-related nasopharynx cancer, and asbestos-related ovarian cancer) (Table 1). The summary RRs for Asian studies are predominantly influenced by Chinese literature. China has experienced a substantial increase in the use of substances such as asbestos and trichloroethylene over the past half-century [31]. Considering the latency period, it is anticipated that the current risk levels in Asian and other developing countries will be higher than those in European nations. However, except for asbestos-related mesothelioma and lung cancer, the meta-analysis RRs for both global and Asian studies were below 2.00, indicating a minimal deviation. Therefore, it can be inferred that the results are unlikely to have been substantially overestimated.

However, the results for formaldehyde-nasopharynx cancer, a rare cancer, the results may have been overestimated because we used odds ratios rather than RRs due to a lack of cohort studies (S16 Table).

In instances where the incidence is low or the RRs are highly variable, the attributable risk of future occupational carcinogenicity is frequently estimated as the change in prevalence of exposure to the occupational carcinogen without the use of imputation for risk [28].

Consequently, in practice, it may be more meaningful to focus on changes in the actual incidence of each cancer type and changes in the prevalence of exposure to each carcinogen when estimating the contributory risk of occupational factors. This would most intuitively inform occupational health policy.

Subsequent to the UK, Canada, and Italy, this is the inaugural study in Asia to develop the K-CAREX program to calculate exposure prevalence by occupational factors [10]. The present study estimated the prevalence of exposures from 2000 to 2015 using the sex turnover rate (male, 4.3; female, 4.1) from the 2008 Korean Employment Information Agency Survey [17], and census data from the Korean General Population Census conducted every 5 years. Therefore, this result can be interpreted as reflecting changes in the size of the workforce by sex in South Korea.

Diesel engine exhaust, which demonstrated the highest prevalence of exposure in our study (total=6.08% in 2000), has emerged as a prominent factor in several studies on occupational carcinogens [32]. This is comparable to the prevalence of diesel engine exhaust exposure calculated in Canada in 2001 using the CAREX Canada [33]. In Korea, diesel engine emissions will continue to make a significant contribution to the occupational cancer PAF through 2030, but the number of workers in diesel engine emissions–related industries has decreased as of 2015. If new cancers are not identified, it is anticipated that the prospective risk of cancer incidence due to future diesel engine exhaust exposure will decrease through the development of emission-reducing devices or electrical equipment [34].

In 2030, nickel-sinonasal cancer was predicted to have the second-highest occupation-related PAF (106 cancer cases and 46 cancer deaths). In a previous study on occupational cancer in Korea by Kim et al. [35], the estimated PAF for sinonasal cancer was the third highest, after those for mesothelioma and lung cancer. A review of the literature from Finland, Canada, Norway, and other countries, mainly among nickel refinery workers, revealed a considerable nickel-induced sinonasal cancer risk range: 2.27 to 28.5 (S12 Table). More recent studies have indicated elevated sinonasal cancer mortality risks [36,37]. Nickel is a sufficient-evidenced occupational factor for lung and nasal cancer. In the present study, nickel exposure was among the top three causes of concern for both men and women. In the Republic of Korea, the industries with the highest prevalence of nickel exposure, as determined by the K-CAREX database, are those involved in the manufacture of transport equipment, including ship and boat building, and metal casting. Although sinonasal cancer is not highly prevalent in Korea, it is necessary to consider the risk in exposed workers.

As of 2015, the prevalence of exposure has decreased significantly. In this regard, asbestos has been the most significantly affected. Korea, which commenced industrialization in the 1970s, had the highest utilization of asbestos in 1996. In Korea, there has been a notable decline in asbestos exposure levels since 2000 compared with the 1990s, which can be attributed to the implementation of more stringent regulations on the use of asbestos [15]. However, according to the Population and Housing Census, the number of employees in asbestos-related industries has remained relatively constant since 2005.

Mesothelioma is a definitively established risk factor for

asbestos exposure. The overall asbestos-related PAF for mesothelioma, which encompasses both environmental and occupational exposures, is estimated to be 91.4% according to the Global Burden of Disease Study (GBD) in 2016 [38]. Previous studies have predicted a significant increase in the incidence of mesothelioma by 2038, based on the use of asbestos in South Korea [39]. Additionally, an upward trend in the expected number of mesothelioma cases and deaths in South Korea was projected to continue until 2030 [21]. Mesothelioma is a cancer that has a long latency period. However, in this study, the latency period of 15 years was set to be the same for solid and leukemia as a common standard for other factors, such as smoking [40], alcohol consumption [41], infection [42], and physical activity [43], in order to allow future studies to combine the contributory risk with other factors. As of 2015, the actual number of mesothelioma cases and deaths in Korea was in the range of 100 (114-139), making it a very rare cancer and therefore a minor contributor to the final attributable risk. However, it is certain that an underestimation occurred. 1,3-Butadiene- and formaldehyde-related cancers also have the potential to be underestimated due to the relatively long lag period.

The prevalence of 1,3-butadiene exposure increased across all sexes; however, the rate remained low at 0.1%. Formaldehyde and crystalline silica dust exposures decreased among men but showed a relative increase among women until 2020. In 2015, formaldehyde was the only carcinogenic factor with a higher prevalence in women than in men. This can be attributed to the increasing number of female workers in formaldehyde-related industries, such as manufacturing, medical practices, and veterinary service industries. Notably, as of 2015, the health sector employed 1.21 million women [14]. A GBD revealed an increase in the prevalence of formaldehyde exposure [38]. In France, the prevalence of formaldehyde exposure among women is nearly double that among men, and nasopharyngeal cancer associated with formaldehyde ranks third among occupational cancer types [36]. Additionally, the AF for formaldehyde-related nasopharyngeal cancer in Italy, at 0.3%, is similar to that observed in this study [32].

In this study, for women, an increase was projected in all carcinogen-related cancer types by 41.6% for cases and 31.7% for deaths by 2030, compared with 2025. A recent GBD study revealed that the turnover rate among women is 1-2 times higher than that among men in several countries, including the United Kingdom and China [38]. In recent years, studies have been conducted in South Korea on the effects of occupational carcinogens (group 2A), such as night shift work and cooking oil fume, on female workers [44-46]. Nevertheless, research on female workers remains limited. The future increase may be more than our estimates for women. Therefore, it is imperative to monitor occupational carcinogens to which women are increasingly exposed.

This is the first Asian study to use the K-CAREX program to estimate occupational cancer risk (PAF) in 2015 and how this changed with reduced exposure from the asbestos ban to 2030. The study is subject to methodological limitations, including an absence of cohort studies and the inability to account for potential confounding variables. Nevertheless, it sought to interpret the factors that require attention from the results and identified key intervention factors by industry, reflecting the evolving industrial environment, and sex ratio of Korea. It is anticipated that the findings will provide a valuable foundation for developing methodologies and indicators to estimate the burden of occupational cancer in Korea.

Electronic Supplementary Material

Supplementary materials are available at Cancer Research and Treatment website (https://www.e-crt.org).

Ethical Statement

This study was approved by the Institutional Review Board of Hanyang University (HYUIRB-202011-006).

Author Contributions

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Collected the data: Kim EM, Koh DH, Park SK, Kim I.
Contributed data or analysis tools: Kim EM, Koh DH, Hong Y, Moon S, Min J, Choi S, Park JH, Lee SG, Kim HC, Park DU, Kim I.
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Conflicts of Interest

Conflict of interest relevant to this article was not reported.

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