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Smoking-attributable Mortality in Korea, 2020: A Meta-analysis of 4 Databases

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Objectives: Estimating the number of deaths caused by smoking is crucial for developing and evaluating tobacco control and smoking cessation policies. This study aimed to determine smoking-attributable mortality (SAM) in Korea in 2020.

Methods: Four large-scale cohorts from Korea were analyzed. A Cox proportional-hazards model was used to determine the hazard ratios (HRs) of smoking-related death. By conducting a meta-analysis of these HRs, the pooled HRs of smoking-related death for 41 diseases were estimated. Population-attributable fractions (PAFs) were calculated based on the smoking prevalence for 1995 in conjunction with the pooled HRs. Subsequently, SAM was derived using the PAF and the number of deaths recorded for each disease in 2020.

Results: The pooled HR for all-cause mortality attributable to smoking was 1.73 for current men smokers (95% confidence interval [CI], 1.53 to 1.95) and 1.63 for current women smokers (95% CI, 1.37 to 1.94). Smoking accounted for 33.2% of all-cause deaths in men and 4.6% in women. Additionally, it was a factor in 71.8% of men lung cancer deaths and 11.9% of women lung cancer deaths. In 2020, smoking was responsible for 53 930 men deaths and 6283 women deaths, totaling 60 213 deaths.

Conclusions: Cigarette smoking was responsible for a significant number of deaths in Korea in 2020. Monitoring the impact and societal burden of smoking is essential for effective tobacco control and harm prevention policies.

Key words: Smoking, Cohort study, Meta-analysis, Cause of death, Mortality

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INTRODUCTION

Globally, the number of smokers is declining. Nonetheless, mortality resulting from smoking continues to be a pressing concern worldwide. It is projected that by 2030, nearly 6 million deaths each year will be attributable to direct smoking, with an additional 1 million due to exposure to secondhand smoke [1]. In Korea, smoking significantly contributes to lung cancer, the leading cause of death. This preventable risk factor is the main contributor to premature mortality. Beyond mortality, the effects of smoking extend to healthcare costs and productivity losses. In 2013, the socioeconomic cost of smoking was substantial, estimated at 7.1 trillion Korean won (5.34 billion US dollars).

The Framework Convention on Tobacco Control of the World Health Organization mandates that signatory countries report smoking-induced deaths biennially through national reports. Collating data on these deaths is pivotal for understanding the long-term repercussions of historical smoking behaviors on today's population, including the degree of harm, and has policy implications. This is also crucial for anticipating and curtailing potential risks associated with current smoking habits. Monitoring smoking-induced fatalities provides public health officials with vital information for mitigating tobacco-induced harm and protecting the well-being of the population.

The smoking prevalence in Korea was notably high in 1997, at 66.2% for men and 6.5% for women. However, these rates have steadily declined over the years. Given that chronic illnesses induced by smoking often cause mortality after 20-30 years [2], current deaths attributed to such ailments likely reflect the high smoking rates of the past. Korean studies assessing smoking-induced fatalities typically employ the population-attributable fraction (PAF) to calculate smoking-attributable mortality (SAM). In earlier research, due to the absence of Korean cohorts, mortality risk data from Japan was adopted [3]. Subsequent research was based on a Korean cohort encompassing civil servants, private school employees, and their health insurance beneficiaries and families [4]. Some cohort studies had relatively brief follow-up durations, often less than 2 decades [4,5], or were restricted to particular diseases [3,4]. This highlights the need for smoking-related death risk estimates and SAM grounded in a large-scale cohort that spans over 20 years and represents the Korean population.

This study aims to investigate SAM in Korea in 2020. We estimated the risk of disease-specific deaths, the PAF across all fatalities, and the number of smoking-related deaths in 2020 using data from the Korean population.

METHODS

This study employed a prevalence-based approach to determine SAM.

Data Source

This study used multiple data sources to estimate smoking-related deaths in Korea. Initially, 4 databases were utilized to calculate hazard ratios (HRs) for SAM (Table 1). The Korea National Health Examination Baseline (KNHEB) cohort includes individuals who participated in the National General Health Screening Program (GHSP) during 2002-2003 [6]. The National Health Insurance Service-Korea Cancer Prevention Study (NHIS-KCPS) is a cohort comprising civil servants, employees of private schools, and their health insurance beneficiaries and families from 1992 to 1995 [4]. KCPS-II includes individuals who underwent general health examinations at one of 18 institutions in the country, with 15 in Seoul and Gyeonggi Province and 3 in other regions, during 1994-2013 [7]. The Korean Metabolic Syndrome Mortality Study (KMSMS) is a retrospective cohort study involving individuals who had health check-ups at 18 general examination centers nationwide from 1994 to 2004 [8]. The smoking-related survey questions used in each database are included in the Supplemental Material 1. All 4 cohorts have informed cause of death statistics issued by Statistics Korea up to 2020.

To calculate SAM, we utilized smoking prevalence data from 1995. Given the 20-year to 30-year time lag between smoking initiation and subsequent mortality, we employed data from the 1995 National Health and Health Behavior Survey conduct-

Table 1. Characteristics of the included cohorts

Cohort name	Baseline survey year	End of follow-up	Sample size (n)			All-cause deaths (n)	
			Total	Men	Women	Men	Women
KNHEB	2002-2003	2020	7 291 311	4 480 843	2 810 468	573 886	306 947
KNHEB-A	2002-2003	2020	6 143 303	3 728 488	2 414 815	492 442	275 324
KNHEB-B	2002-2003	2020	1 148 008	752 355	395 653	81 444	31 623
NHIS-KCPS	1992-1999	2020	1 327 003	845 932	481 071	175 745	18 817
KCPS-II	1994-2013	2020	226 958	134 633	92 325	6146	442
KMSMS	1996-2004	2020	304 007	173 091	130 916	16 518	1278

KNHEB-A, Korea National Health Examination Baseline (analytical subset); KNHEB-B, Korea National Health Examination Baseline (duplicate data from NHIS-KCPS); NHIS-KCPS, National Health Insurance Service-Korea Cancer Prevention Study; KCPS-II, Korea Cancer Prevention Study-II; KMSMS, Korean Metabolic Syndrome Mortality Study.

ed by the Korea Institute for Health and Social Affairs. These figures were used by the Korea Disease Control and Prevention Agency to assess smoking-related risks in 2019. We referred to smoking rates for individuals aged 30-69 years, as the survey did not include those aged 70 years or older. In 1995, the smoking rates for men were as follows: current smokers, 65.6%; former smokers, 16.5%; and non-smokers, 17.9%. For women, the respective rates were 6.4%, 1.6%, and 92.0% (Supplemental Material 2).

To calculate SAM in 2020, disease-specific death data were used from Statistics Korea's cause of death statistics [9]. Statistics Korea compiles nationwide death reports, including the year of death, age, and cause of death based on International Classification of Diseases, 10th revision codes. These reports are made available to the Korean public.

Data Extraction

The analysis was restricted to men and women adults aged 30 years and older. Based on smoking data obtained at the start of the cohort study, participants were categorized as current smokers, former smokers, or non-smokers. In total, 41 diseases strongly correlated with smoking, as identified in the Surgeon General's Report [10] and prior Korean studies, were included in the analysis. Since the KNHEB cohort is extremely large, to avoid duplication of data from the NHIS-KCPS—which includes civil servants, private school staff, and their health insurance beneficiaries and families registered under the National Health Insurance Service—individuals within the NHIS-KCPS cohort were excluded from the KNHEB dataset. This revised dataset was designated as KNHEB-A, representing the analytical subset of the KNHEB cohort.

Statistical Analysis

To determine SAM, we utilized a prevalence-based approach employing the PAF. Initially, a Cox proportional hazards model was used to derive HRs for mortality for 41 smoking-related diseases. The HRs were adjusted for age and alcohol consumption and were calculated separately for current and former smokers, with non-smokers as the baseline. HRs for each disease were derived from the 4 databases individually. A meta-analysis was performed using the HR values obtained from each database to calculate the integrated estimates. Because the study populations in the included cohorts were not identical, and given our intention to generalize findings to the wider population, a random-effects model was used. Heterogeneity between studies was evaluated using the Higgins I^2 test [11].

The pooled HRs and the 1995 smoking prevalence data were used to estimate the PAFs as follows [12]:

$$\mathrm{PAF} = \frac{(p_{current\ smoker} \times HR_{current\ smoker}) + (p_{former\ smoker} \times HR_{former\ smoker}) + p_{never\ smoker} - 1}{(p_{current\ smoker} \times HR_{current\ smoker}) + (p_{former\ smoker} \times HR_{former\ smoker}) + p_{never\ smoker}}$$

where p represents the prevalence of current smokers, former smokers, and never smokers. To obtain the final SAM, the disease-specific PAFs were multiplied by the respective disease-specific mortality figures from 2020. For sensitivity analysis, SAMs were computed using gender-specific smoking rates from 2001, 2005, and 2010 [13], with time lags of 19 years, 15 years, and 10 years, respectively. A comparative examination was conducted to assess the impact of these different periods on the analysis. The prevalence rate for 2001 was employed because it was the closest available data point to the year 2000.

Ethics Statement

The Institutional Review Board of Seoul National University approved KNHEB (IRB No. E2405/002-011). The Institutional Review Board of Yonsei University granted approval for NHIS-KCPS, KCPS-II, KMSMS (NHIS-KCPS IRB No. 4-2001-0029, KCPS-II IRB No. 4-2011-0277, KMSMS IRB No. 4-2007-0065).

RESULTS

Cohort Characteristics

The smoking-related attributes of the participants included in the HR calculations for each cohort are presented in Table 2. In the KNHEB cohort, the current smoking rate was 30.7%, while the former smoker rate was 9.7%. Among current smokers, the majority consumed 0.5-1.0 pack per day, and the most prevalent smoking duration was 10-19 years. For former smokers, the most common smoking duration was also 10-19 years. Within the NHIS-KCPS, the current smoking rate was 38.9% among men, and the rate of former smokers was 14.0%. The majority of current smokers smoked 0.5-1.0 pack daily, and 10-19 years was the most frequent smoking duration. In the KCPS-II cohort, the current smoking rate was 28.7%, and the former smoking rate was 18.8%. Among current smokers, the largest group smoked 1-2 packs daily, and the most common smoking duration was 10-19 years. For former smokers, the most common smoking duration was also 10-19 years. In the KMSMS cohort, the current smoking rate was 31.6%, and the former smoking rate was 17.7%. Among current smokers, the largest group

Table 2. Smoking-related characteristics of the included cohorts

Characteristics	KNHEB-A			NHIS-KCPS			KCPS-II			KMSMS		
	Men	Women	Total	Men	Women	Total	Men	Women	Total	Men	Women	Total
Smoking status												
Current smokers	1 808 209 (48.5)	75 950 (3.1)	1 884 159 (30.7)	494 719 (58.5)	20 840 (4.3)	515 559 (38.9)	61 329 (45.6)	3893 (4.2)	65 223 (28.7)	89 169 (51.5)	6961 (5.3)	96 130 (31.6)
Former smokers	567 439 (15.2)	30 775 (1.3)	598 214 (9.7)	175 611 (20.8)	10 543 (2.2)	186 154 (14.0)	37 833 (28.1)	4908 (5.3)	42 741 (18.8)	46 876 (27.1)	6936 (5.3)	53 812 (17.7)
Non-smokers	1 352 840 (36.3)	2 308 090 (95.6)	3 660 930 (59.6)	175 602 (20.8)	449 688 (93.5)	625 290 (47.1)	35 471 (26.4)	83 523 (90.5)	118 994 (52.4)	37 046 (21.4)	117 019 (89.4)	154 065 (50.7)
Current smokers (n)	1 808 209	75 950	1 884 159	494 719	20 840	515 559	61 329	3894	65 223	89 169	6961	96 130
Smoking volume (pack/day)												
<0.5	404 325 (22.4)	48 475 (63.8)	452 800 (24.0)	15 749 (3.2)	4072 (19.5)	19 821 (3.8)	7955 (13.0)	1574 (40.4)	929 (14.6)	8850 (9.9)	2386 (34.3)	11 236 (11.7)
0.5-1.0	1 002 349 (55.4)	21 523 (28.3)	1 023 872 (54.3)	330 179 (66.7)	14 486 (69.5)	344 665 (66.9)	24 168 (39.4)	1306 (33.5)	25 474 (39.1)	28 114 (31.5)	2383 (34.2)	30 497 (31.7)
1.0-2.0	373 471 (20.7)	4456 (5.9)	377 927 (20.1)	148 791 (30.1)	2282 (11.0)	151 073 (29.3)	26 195 (42.7)	589 (15.1)	26 784 (41.1)	44 169 (49.5)	1355 (19.5)	45 524 (47.4)
>2.0	21 896 (1.2)	355 (0.5)	22 251 (1.2)	-	-	-	1802 (2.9)	41 (1.1)	1843 (2.8)	4280 (4.8)	76 (1.1)	4356 (4.5)
Missing	6168 (0.3)	1141 (1.5)	7309 (0.4)	-	-	-	1209 (2.0)	384 (9.9)	1593 (2.4)	3756 (4.2)	761 (10.9)	4517 (4.7)
Smoking duration (y)												
0-4	56 684 (3.1)	9816 (12.9)	66 500 (3.5)	14 690 (3.0)	2918 (14.0)	17 608 (3.4)	1135 (1.9)	323 (8.3)	1458 (2.2)	7841 (8.8)	1095 (15.7)	8936 (9.3)
5-9	195 124 (10.8)	12 444 (16.4)	207 568 (11.0)	32 017 (6.5)	2178 (10.5)	34 195 (6.6)	2862 (4.7)	689 (17.7)	3551 (5.4)	1168 (1.3)	810 (11.6)	1978 (2.1)
10-19	786 036 (43.5)	20 638 (27.2)	806 674 (42.8)	152 871 (30.9)	2837 (13.6)	155 708 (30.2)	24 207 (39.5)	1573 (40.4)	25 780 (39.5)	20 134 (22.6)	2210 (31.8)	22 344 (23.2)
20-29	403 798 (22.3)	12 819 (16.9)	416 617 (22.1)	114 066 (23.1)	3391 (16.3)	117 457 (22.8)	19 968 (32.6)	626 (16.1)	20 594 (31.6)	26 166 (29.3)	1062 (15.3)	27 228 (28.3)
≥30	317 863 (17.6)	17 446 (23.0)	335 309 (17.8)	78 329 (15.8)	4997 (24.0)	83 326 (16.2)	10 344 (16.9)	231 (5.9)	10 575 (16.2)	17 396 (19.5)	403 (5.8)	17 799 (18.5)
Missing	48 704 (2.7)	2787 (3.7)	51 491 (2.7)	102 746 (20.8)	4519 (21.7)	107 265 (20.8)	2813 (4.6)	452 (11.6)	3265 (5.0)	16 464 (18.5)	1381 (19.8)	17 845 (18.6)
Former smokers (n)	567 439	30 775	598 214	175 611	10 543	186 154	37 833	4908	42 741	46 876	6936	53 812
Smoking duration (y)												
0-4	68 117 (12.0)	12 482 (40.6)	80 599 (13.5)	24 244 (13.8)	2294 (21.8)	26 538 (14.3)	3290 (8.7)	558 (11.4)	3848 (9.0)	3675 (7.8)	388 (5.6)	4063 (7.6)
5-9	112 492 (19.8)	6668 (21.7)	119 160 (19.9)	19 355 (11.0)	966 (9.2)	20 321 (10.9)	4392 (11.6)	489 (10.0)	4881 (11.4)	1822 (3.9)	265 (3.8)	2087 (3.9)
10-19	178 568 (31.5)	3985 (12.9)	182 553 (30.5)	39 355 (22.4)	1591 (15.1)	40 946 (22.0)	11 799 (31.2)	389 (7.9)	12 188 (28.5)	7744 (16.5)	332 (4.8)	8076 (15.0)
20-29	87 095 (15.3)	1853 (6.0)	88 948 (14.9)	23 523 (13.4)	1059 (10.0)	24 582 (13.2)	7567 (20.0)	118 (2.4)	7685 (18.0)	7287 (15.6)	138 (2.0)	7425 (13.8)
≥30	55 047 (9.7)	1511 (4.9)	56 558 (9.5)	14 838 (8.5)	926 (8.8)	15 764 (8.5)	3943 (10.4)	60 (1.2)	4003 (9.4)	4385 (9.4)	52 (0.8)	4437 (8.3)
Missing	66 120 (11.7)	4276 (13.9)	70 396 (11.8)	54 296 (30.9)	3707 (35.2)	58 003 (31.2)	6842 (18.1)	3294 (67.1)	10 136 (23.7)	21 963 (46.9)	5761 (83.1)	27 724 (51.5)

Values are presented as number (%).
KNHEB-A, Korea National Health Examination Baseline (analytical subset); NHIS-KCPS, National Health Insurance Service-Korea Cancer Prevention Study; KCPS-II, Korea Cancer Prevention Study-II; KMSMS, Korean Metabolic Syndrome Mortality Study.

smoked 1-2 packs per day, and 20-29 years was the most common smoking duration. Among former smokers, the largest proportion had a smoking duration of 10-19 years. The 4 cohorts showed differences in general characteristics, as detailed in the Supplemental Material 3.

Results of Meta-analysis

The pooled HRs, estimated using each HRs from 4 cohorts by disease (Supplemental Materials 4 and 5), for all-cause mortality exceeded 1.5 for current smokers and 1.0 for former smokers. Among men, current smokers exhibited an elevated overall risk of cancer, as well as an increased risk of esophageal cancer, lung cancer, stroke, atherosclerosis, coronary obstructive pulmonary disease (COPD), and pneumonia. Former smokers had a higher risk of all-cause death, as well as a higher overall cancer risk and increased risk of laryngeal cancer, lung cancer, ischemic heart disease (IHD), and COPD. In women, current smokers had higher HRs for cancer overall, as well as for cancers of the esophagus, larynx, lung, and bladder, IHD, atherosclerosis, COPD, and pneumonia. Former smokers showed increased HRs for all-cancer, cancers of the esophagus and lung, IHD, atherosclerosis, COPD, and pneumonia. Heterogeneity in pooled HR was observed in some diseases in both genders (Tables 3 and 4).

Population-attributable Fraction

The PAF, calculated using pooled HRs and smoking prevalence data from 1995, was 33.2% for men and 4.5% for women for all-cause death. For men, the PAF exceeded 50% for esophageal cancer, laryngeal cancer, lung cancer, and COPD, and surpassed 30% for all-cause death, all cancers, oropharyngeal cancer, stomach cancer, bladder cancer, IHD, and atherosclerosis. For women, the PAFs for laryngeal cancer, esophageal cancer, lung cancer, atherosclerosis, COPD, and ulcers were greater than 10% (Table 5).

Smoking-attributable Mortality

In 2020, smoking was responsible for 60 213 deaths (53 930 in men and 6283 in women). For men, lung cancer was the predominant cause of SAM, accounting for approximately 10 000 deaths, followed by pneumonia, IHD, stroke, and liver cancer (each with more than 2000 deaths). Among women, lung cancer was the leading cause of SAM (over 500 deaths), with pneumonia, stroke, and IHD each resulting in more than 400 deaths (Table 5).

Applying smoking rates for 2001, 2005, and 2010 resulted in SAM values of 56 839 (51 461 men, 5378 women), 54 684 (47 488 men, 7196 women), and 54 081 (45 902 men, 8179 women), respectively (Supplemental Materials 6 and 7).

DISCUSSION

This is the first study to integrate risk estimates and calculate SAM for smoking-associated diseases using 4 large Korean cohorts. There were 60 213 smoking-induced deaths in 2020 (53 930 men and 6283 women). The disease with the highest mortality rate was lung cancer, with 10 499 deaths (9921 men and 578 women), followed by pneumonia, IHD, and stroke.

To calculate HRs, this study utilized 4 databases, as previously noted. The NHIS-KCPS, established in 1992, has certain limitations as it predominantly consists of civil service personnel, educators, and their beneficiaries. To address these limitations, data from 3 additional databases were used: the KNHEB cohort, which includes more than 10.4 million individuals who underwent the National Health Insurance Service GHSP in 2002-2003 [14], and the KCPS-II and KMSMS databases. Although the latter 2 databases are more limited in scope, they provide greater temporal coverage, thereby helping to mitigate the limitations of the NHIS-KCPS. The representativeness of the HRs derived from these extensive cohorts was confirmed through a thorough meta-analysis.

In the study of Jung et al. [15] that was published in 2013, which used PAFs to determine SAM for Koreans, a meta-analysis of the HRs for 41 diseases was conducted based on both the NHIS-KCPS and the KMSMS. For current men smokers, the HRs for death were as follows: all-cause death, 1.75 (95% confidence interval [CI], 1.43 to 2.12); all cancers, 1.98 (95% CI, 1.60 to 2.44); esophageal cancer, 2.59 (95% CI, 2.19 to 3.01); lung cancer, 4.80 (95% CI, 4.02 to 5.73); IHD, 2.04 (95% CI, 1.55 to 2.68); stroke, 1.57 (95% CI, 1.22 to 2.03); and pneumonia, 1.51 (95% CI, 1.34 to 1.71). These figures align closely with this study's findings. However, the HR for atherosclerosis in this study (2.38; 95% CI, 1.85 to 3.07) was lower than in Jung et al. [15] (3.55; 95% CI, 2.66 to 4.73), while that for COPD (3.34; 95% CI, 1.88 to 5.93) was higher than in Jung et al. (2.46; 95% CI, 2.16 to 2.22). For current women smokers, the HRs were mostly consistent for all-cause mortality, lung cancer, and IHD, but differences were noted in esophageal cancer, COPD, and pneumonia HRs. Although there were discrepancies in HRs across diseases, in most cases the difference was <1.0. The consistent outcomes

Table 3. HRs for death related to smoking in men

Diseases	ICD-10	Former smokers			Current smokers		
		HR (95% CI)	τ^2	I^2 (%)	HR (95% CI)	τ^2	I^2 (%)
All-cause		1.11 (1.05, 1.17)	0.00	98	1.73 (1.53, 1.95)	0.01	98
All cancers		1.20 (1.14, 1.25)	0.00	90	1.99 (1.72, 2.30)	0.02	98
Oropharynx	C00-C14	1.11 (0.94, 1.31)	0.01	14	1.90 (1.68, 2.15)	0.01	17
Esophagus	C15	1.21 (1.00, 1.46)	0.02	57	2.96 (1.92, 4.56)	0.15	91
Stomach	C16	1.11 (0.99, 1.24)	0.01	83	1.66 (1.46, 1.89)	0.01	90
Small intestine	C17	1.14 (0.93, 1.40)[1]	<0.001	5	1.50 (1.29, 1.76)[1]	<0.001	45
Colon	C18	1.08 (0.99, 1.17)	0.00	28	1.14 (1.05, 1.24)	0.00	56
Rectum	C19, C20	1.07 (1.01, 1.14)	0.00	0	1.30 (1.24, 1.37)	0.00	0
Liver	C22	1.14 (1.01, 1.28)	0.01	94	1.61 (1.34, 1.92)	0.03	87
Gallbladder	C23, C24	1.09 (1.00, 1.19)	0.00	34	1.24 (1.10, 1.40)	0.01	76
Pancreas	C25	0.97 (0.83, 1.14)	0.02	75	1.46 (1.40, 1.51)	0.00	0
Larynx	C32	1.71 (1.16, 2.50)	0.06	56	4.14 (2.41, 7.11)	0.18	83
Lung	C34	1.70 (1.50, 1.92)	0.01	88	4.71 (3.56, 6.25)	0.08	99
Brain	C71	1.08 (0.98, 1.19)	0.00	47	1.16 (0.88, 1.52)	0.05	62
Thyroid	C73	0.79 (0.33, 1.92)	0.55	69	1.07 (0.74, 1.55)	0.06	44
Leukemia	C91-C95	1.06 (0.98, 1.15)	0.00	0	1.16 (1.05, 1.29)	0.00	8
Bladder	C67	1.40 (1.10, 1.78)	0.03	75	1.85 (1.49, 2.32)	0.03	78
Kidney	C64	1.00 (0.84, 1.21)	0.02	44	1.25 (1.15, 1.35)	0.00	0
Prostate	C61	0.96 (0.88, 1.06)	0.00	37	1.04 (0.96, 1.12)	0.00	46
Breast	C50	1.10 (0.58, 2.07)[2]	0.00	0	1.52 (0.94, 2.47)[2]	0.00	0
Cervix	C53	-	-	-	-	-	-
Ovary	C56	-	-	-	-	-	-
Circulatory							
Hypertensive disease	I10-I13	1.00 (0.76, 1.31)	0.05	88	1.40 (1.27, 1.54)	0.00	30
Ischemic heart disease	I20-I25	1.26 (1.10, 1.44)	0.01	86	1.92 (1.67, 2.21)	0.02	73
Arrhythmia	I47-I49	1.04 (0.86, 1.25)	0.01	39	1.22 (1.12, 1.32)	0.00	0
Heart failure	I50	1.02 (0.95, 1.10)	0.00	0	1.37 (1.26, 1.49)	0.00	0
Stroke	I60-I69	0.98 (0.93, 1.03)	0.00	43	1.52 (1.32, 1.74)	0.02	82
Atherosclerosis	I70-I74	1.22 (1.03, 1.44)	0.01	1	2.38 (1.85, 3.07)	0.04	77
Other							
Diabetes mellitus	E10-E14	1.06 (0.93, 1.20)	0.01	78	1.59 (1.37, 1.84)	0.02	67
Organic, including symptomatic, mental disorders	F00-F09	0.95 (0.83, 1.08)[2]	0.01	57	1.32 (1.14, 1.53)[2]	0.01	75
Sudden death	R96	0.91 (0.74, 1.13)	0.02	48	1.48 (1.35, 1.62)	<0.001	43
Aging	R54	1.01 (0.97, 1.05)	<0.001	24	1.41 (1.37, 1.45)	0.00	0
COPD	J44	1.84 (1.38, 2.46)	0.06	88	3.34 (1.88, 5.93)	0.31	97
Tuberculosis	A15-A19	1.18 (0.95, 1.43)[2]	0.02	83	1.42 (1.28, 1.58)[2]	0.00	55
Pneumonia	J09-J18	1.13 (1.01, 1.26)	0.01	81	1.52 (1.32, 1.74)	0.01	73
Ulcer	K25-K27	1.06 (0.87, 1.29)	0.00	4	2.03 (1.77, 2.34)	0.00	0
Liver cirrhosis	K74	0.97 (0.78, 1.21)	0.03	85	1.56 (1.35, 1.81)	0.01	79
Accident	V01-V99	0.86 (0.82, 0.89)[1]	0.00	0	1.19 (1.08, 1.32)[1]	0.01	83
Poisoning	X40-X49	0.78 (0.60, 1.00)[2]	0.00	0	1.54 (1.15, 2.07)[2]	0.03	57
Unspecified causes	X58-X59	1.07 (0.96, 1.21)[2]	0.00	0	1.41 (1.29, 1.55)[2]	0.00	0
Suicide	X60-X84	0.99 (0.85, 1.15)[2]	0.01	91	1.42 (1.31, 1.54)[2]	0.00	80
Homicide	X85-Y09	0.93 (0.73, 1.17)[2]	0.00	0	1.33 (1.13, 1.58)[2]	0.00	0
Injury undetermined	Y10-Y34	0.97 (0.89, 1.05)[2]	0.00	0	1.43 (1.34, 1.52)[2]	0.00	6

ICD-10, International Classification of Diseases, 10th revision; HR, hazard ratio; CI, confidence interval; KNHEB-A, Korea National Health Examination Baseline (analytical subset); NHIS-KCPS, National Health Insurance Service-Korea Cancer Prevention Study; KCPS-II, Korea Cancer Prevention Study-II; KMSMS, Korean Metabolic Syndrome Mortality Study; COPD, chronic obstructive pulmonary disease.
[1]Results from 3 databases (KNHEB, NHIS-KCPS, and KMSMS).
[2]Results from 2 databases (KNHEB and NHIS-KCPS).

Table 4. HRs for death related to smoking in women

Diseases	ICD-10	Former smokers			Current smokers		
		HR (95% CI)	τ^2	I^2 (%)	HR (95% CI)	τ^2	I^2 (%)
All-cause		1.44 (1.13, 1.83)	0.06	94	1.63 (1.37, 1.94)	0.03	98
All cancers		1.31 (1.11, 1.54)	0.02	79	1.56 (1.36, 1.80)	0.02	95
Oropharynx	C00-C14	0.92 (0.60, 1.42)[1]	0.00	0	1.50 (1.12, 2.02)[1]	0.00	0
Esophagus	C15	2.68 (1.67, 4.31)[1]	<0.001	56	2.70 (1.57, 4.64)[1]	0.10	48
Stomach	C16	1.11 (0.99, 1.25)	<0.001	0	1.30 (1.09, 1.54)	0.02	65
Small intestine	C17	1.09 (0.13, 8.77)[2]	1.78	75	1.07 (0.28, 4.16)[2]	0.77	78
Colon	C18	1.16 (1.00, 1.35)	0.00	0	1.27 (1.07, 1.49)	0.01	57
Rectum	C19, C20	1.30 (1.07, 1.58)	0.00	0	1.25 (1.03, 1.51)	0.01	20
Liver	C22	1.29 (1.14, 1.46)	0.00	0	1.47 (1.18, 1.83)	0.03	79
Gallbladder	C23, C24	1.24 (0.70, 2.19)	0.28	81	1.29 (1.08, 1.53)	0.01	34
Pancreas	C25	1.04 (0.73, 1.47)	0.08	79	1.28 (1.00, 1.64)	0.04	76
Larynx	C32	3.48 (0.92, 13.23)[2]	0.60	64	9.14 (6.18, 13.52)[2]	0.00	0
Lung	C34	1.59 (1.44, 1.75)	<0.001	53	2.96 (1.98, 4.41)	0.14	85
Brain	C71	0.98 (0.69, 1.40)	0.01	30	0.99 (0.79, 1.24)	0.00	0
Thyroid	C73	1.39 (0.94, 2.07)	0.00	0	1.01 (0.74, 1.38)	0.00	0
Leukemia	C91-C95	0.87 (0.63, 1.21)[1]	0.00	0	0.97 (0.70, 1.35)	0.04	24
Bladder	C67	1.33 (0.93, 1.91)[1]	0.00	0	1.84 (1.48, 2.29)[1]	0.00	0
Kidney	C64	1.52 (1.04, 2.23)[1]	0.00	0	0.98 (0.72, 1.34)[1]	0.00	0
Prostate	C61	-	-	-	-	-	-
Breast	C50	1.29 (1.07, 1.56)	0.00	0	1.12 (0.86, 1.47)	0.04	48
Cervix	C53	1.10 (0.82, 1.49)[1]	0.00	0	1.82 (1.55, 2.14)	0.00	0
Ovary	C56	1.08 (0.84, 1.39)[1]	0.00	0	1.10 (0.92, 1.33)	0.00	0
Circulatory							
Hypertensive disease	I10-I13	1.38 (1.14, 1.68)	0.02	40	1.57 (1.31, 1.88)	0.02	68
Ischemic heart disease	I20-I25	1.47 (1.07, 2.02)	0.08	71	2.00 (1.85, 2.16)	0.00	56
Arrhythmia	I47-I49	1.10 (0.86, 1.42)	0.00	0	1.59 (1.38, 1.84)	0.00	0
Heart failure	I50	1.42 (1.15, 1.75)	0.02	39	1.70 (1.41, 2.04)	0.02	61
Stroke	I60-I69	1.26 (1.06, 1.50)	0.02	67	1.60 (1.29, 1.98)	0.04	87
Atherosclerosis	I70-I74	1.94 (1.49, 2.53)	0.01	38	2.83 (1.93, 4.14)	0.09	67
Other							
Diabetes mellitus	E10-E14	1.39 (1.27, 1.52)	0.00	0	1.57 (1.46, 1.68)	0.00	16
Organic, including symptomatic, mental disorders	F00-F09	1.38 (1.14, 1.68)[2]	0.01	56	1.40 (1.23, 1.59)[2]	0.00	56
Sudden death	R96	0.93 (0.59, 1.47)	0.00	0	1.65 (1.30, 2.08)	0.00	0
Aging	R54	1.43 (1.28, 1.59)	0.01	50	1.68 (1.04, 2.70)	0.18	99
COPD	J44	2.41 (1.69, 3.44)	0.06	72	3.92 (2.94, 5.21)[1]	0.05	76
Tuberculosis	A15-A19	1.44 (0.93, 2.24)[2]	0.07	69	1.40 (1.20, 1.64)[2]	0.00	0
Pneumonia	J09-J18	1.37 (1.24, 1.51)	0.00	28	1.67 (1.45, 1.92)	0.01	73
Ulcer	K25-K27	2.64 (0.54, 12.94)[1]	1.62	73	2.77 (2.22, 3.46)[1]	0.00	0
Liver cirrhosis	K74	1.35 (1.09, 1.67)	<0.001	0	1.61 (1.23, 2.09)	0.03	49
Accident	V01-V99	1.10 (0.94, 1.28)[1]	0.00	0	1.51 (0.97, 2.36)[1]	0.15	93
Poisoning	X40-X49	1.74 (0.83, 3.66)[2]	0.00	0	2.18 (1.39, 3.41)[2]	0.00	0
Unspecified causes	X58-X59	1.15 (0.90, 1.47)[2]	0.00	0	1.66 (1.19, 2.32)[2]	0.05	81
Suicide	X60-X84	1.48 (1.23, 1.79)[2]	0.01	38	1.78 (1.44, 2.21)[2]	0.02	77
Homicide	X85-Y09	1.60 (0.71, 3.61)[2]	0.14	40	2.33 (1.68, 3.22)[2]	0.00	0
Injury undetermined	Y10-Y34	1.06 (0.78, 1.43)[2]	0.00	0	1.34 (0.97, 1.86)[2]	0.04	68

ICD-10, International Classification of Diseases, 10th revision; HR, hazard ratio; CI, confidence interval; KNHEB-A, Korea National Health Examination Baseline (analytical subset); NHIS-KCPS, National Health Insurance Service-Korea Cancer Prevention Study; KCPS-II, Korea Cancer Prevention Study-II; KMSMS, Korean Metabolic Syndrome Mortality Study; COPD, chronic obstructive pulmonary disease.
[1]Results from 3 databases (KNHEB, NHIS-KCPS, and KMSMS).
[2]Results from 2 databases (KNHEB and NHIS-KCPS).

Table 5. Population-attributable fraction (PAF) and smoking-attributable mortality (SAM) in 2020

Diseases	ICD-10	PAF (%)		Deaths in 2020		SAM	
		Men	Women	Men	Women	Men	Women
All-cause	-	33.2	4.6	162 444	138 031	53 930	6283
All cancers	-	40.5	4.0	50 555	31 206	20 478	1237
Oropharynx	C00-C14	37.8	3.0	969	308	366	9
Esophagus	C15	56.8	12.0	1403	160	798	19
Stomach	C16	31.0	2.1	4804	2686	1492	55
Small intestine	C17	26.1	0.6	201	114	52	1
Colon	C18	9.6	1.9	2854	2553	273	49
Rectum	C19, C20	17.5	2.0	2159	1281	377	26
Liver	C22	29.6	3.4	7810	2749	2311	92
Gallbladder	C23, C24	14.6	2.2	2783	2406	407	52
Pancreas	C25	22.8	1.8	3449	3322	786	61
Larynx	C32	68.5	36.1	310	11	212	4
Lung	C34	71.8	11.9	13 809	4843	9921	578
Brain	C71	10.3	0.0	710	593	73	0
Thyroid	C73	1.5	0.7	128	237	2	2
Leukemia	C91-C95	10.5	0.0	976	734	102	0
Bladder	C67	38.5	5.6	1235	358	476	20
Kidney	C64	14.2	0.7	763	311	108	2
Prostate	C61	1.9	-	2193	-	41	-
Breast	C50	26.4	1.3	20	2712	5	34
Cervix	C53	-	5.2	-	807	-	42
Ovary	C56	-	0.8	-	1362	-	11
Circulatory							
Hypertensive disease	I10-I13	20.8	4.1	1996	4103	415	168
Ischemic heart disease	I20-I25	39.2	6.7	7933	6091	3111	408
Arrhythmia	I47-I49	12.9	3.8	867	1162	112	44
Heart failure	I50	19.8	4.9	2419	4833	479	237
Stroke	I60-I69	25.3	4.1	10 596	11 209	2676	458
Atherosclerosis	I70-I74	48.6	11.7	809	632	393	74
Other							
Diabetes mellitus	E10-E14	28.4	4.1	4306	4126	1224	169
Organic, including symptomatic, mental disorders	F00-F09	16.8	3.1	1082	2049	182	64
Sudden death	R96	23.0	3.9	499	378	115	15
Aging	R54	21.3	4.8	5150	10 673	1096	515
COPD	J44	62.6	17.4	2856	1130	1788	196
Tuberculosis	A15-A19	23.4	3.2	840	511	197	16
Pneumonia	J09-J18	26.4	4.7	12 186	10 284	3221	479
Ulcer	K25-K27	40.8	12.3	256	244	104	30
Liver cirrhosis	K74	26.6	4.3	1331	869	354	37
Accident	V01-V99	9.4	3.3	2644	922	249	31
Poisoning	X40-X49	24.2	8.1	168	59	41	5
Unspecified causes	X58-X59	22.1	4.3	546	828	121	36
Suicide	X60-X84	21.7	5.5	8080	3327	1751	182
Homicide	X85-Y09	17.1	8.7	166	140	28	12
Injury undetermined	Y10-Y34	21.6	2.3	1035	540	224	12

ICD-10, International Classification of Diseases, 10th revision; COPD, chronic obstructive pulmonary disease.

might be due to the similar follow-up durations, of roughly 20 years, between the cohort in the research of Jung et al. [15] and the KNHEB cohort analyzed in this study.

In Katanoda et al. [16]'s 2008 study, which determined the HRs for smoking-associated disease mortality among the Japanese population, a meta-analysis of 3 large-scale Japanese cohort studies was performed. The age-adjusted HRs for current men smokers were as follows: all-cause mortality, 1.63 (95% CI, 1.56 to 1.70); all cancer, 1.97 (95% CI, 1.83 to 2.13); and lung cancer, 4.79 (95% CI, 3.88 to 5.92). These HRs closely align with those in our study. However, for conditions such as laryngeal cancer (HR, 5.47; 95% CI, 1.29 to 23.11), bladder cancer (HR, 5.35; 95% CI, 2.47 to 11.57), and IHD (HR, 2.18; 95% CI, 1.79 to 2.66), the HRs were slightly lower in this study. For women, excluding COPD (HR, 3.55; 95% CI, 1.53 to 8.21), the HRs were similar or slightly higher in Katanoda et al. [16]'s study. Their cohorts, predominantly from 1983 to 1993, had follow-up durations of 8.5-10.4 years, which is shorter than the follow-up in our study. Despite this, the HRs reported by Katanoda et al. [16] were higher. This could be due to a change in smoking intensity. Between 1950 and 1980, while Japan experienced an increase in smoking intensity, there was a decline in smoking prevalence, leading to an increase in per capita tobacco use [17]. This might explain the persistently high risk of smoking-related mortality even within shorter follow-up intervals.

In the present study, a high level of heterogeneity was found in some pooled HRs. This heterogeneity could be attributed to several factors.

First, differences in the baseline survey years and follow-up periods across cohorts might have contributed to the observed heterogeneity. Notably, although the KNHEB cohort was the largest in scale, it used smoking data from a survey conducted in 2002-2003 with a maximum observation period of 18 years. In contrast, the NHIS-KCPS, KCPS-II, and KMSMS cohorts had baseline survey years spanning 1992-1999, 1994-2013, and 1996-2004, respectively, with maximum observation periods of 28 years, 26 years, and 24 years, respectively. Each of these periods exceeded 20 years. In the KNHEB cohort, the HRs showed an overall tendency to be smaller than those observed for the other 3 cohorts.

Second, smoking quantity might have affected the HRs. As the smoking quantity increases among current smokers, the risk of death from cancer, cardiovascular diseases, and other smoking-related diseases also rises [18]. The proportion of smokers consuming more than 1 pack a day was higher in NHIS-KCPS, KCPS-II, and KMSMS at 29.3%, 43.9%, and 51.9%, respectively, compared to 21.3% in KNHEB. This suggests that differences in HR values could be due to this disparity in smoking amounts.

Third, considering the significant reduction in the risk of lung cancer incidence in response to decreased smoking and increased smoking cessation [19], changes in smoking habits after the baseline survey in each cohort may have contributed to differences in HRs due to the cumulative risk of smoking-related mortality.

Fourth, advancements in medical technology in Korea have significantly improved survival rates, which increased from 42.9% in 1993-1995 to 70.3% in 2014-2018 [20]. The more favorable prognosis in recent years may have contributed to the decreased HRs in the latest cohort.

However, compared with other studies with shorter observation periods, smaller sample sizes or specific population groups [5,15,21], this study derived more representative HRs from large Korean cohorts observed over more than a decade. Additionally, the random-effect model assumes variability in exposure estimates across studies. Therefore, the characteristics identified as sources of heterogeneity were appropriately addressed.

In the 2013 study of Jung et al. [15], which used pooled HRs similar to our approach and analyzed 1985 smoking rates, the PAFs were higher than in our study. However, the changes in smoking rates in Korea—with decreases from 71.1% in 1985 to 65.6% in 1995 in men and from 10.7% to 6.4% in women—had a greater impact than the differences in the HRs.

In Katanoda et al. [16]'s 2008 study, the PAF for all-cause deaths was 27.8% for men and 6.7% for women. For all cancer deaths, the PAF was 38.6% for men and 5.2% for women. For lung cancer, the PAF was 69.2% for men and 19.8% for women. For IHD, the PAF was 44.1% for men and 15.2% for women. These figures were slightly lower than those for men in our study but slightly higher than those for women. The differences in PAFs might be attributed to the differing smoking rates in Japan, rather than the higher HRs in Katanoda et al. [16]'s study. Specifically, the current smoking rate in Japan was reported as 54.4% for men and 8.1% for women, while the past smoking rates were 25.1% and 2.4%, respectively. The rates for Japanese men smokers are lower than those for their Korean counterparts, but the reverse is true for Japanese women smokers.

Ma et al. [22] calculated PAFs and SAM for individual United States states and reported PAFs of 20.6% and 15.1% for adult (aged >35 years) men and women, respectively. The rate for men was lower than that in our study; however, the reverse was true for women. They analyzed relatively recent (2014) data from the Behavior Risk Factor Surveillance System, which could explain the differences.

When calculating the PAF, it is crucial to consider the proportions of current, former, and non-smokers, as the chosen smoking prevalence at a specific time point significantly influences the SAM. Some studies have applied smoking prevalence from the year of interest for mortality [23] or have used smoking rates at the time of enrollment from a single cohort. However, some Korean studies typically do not derive from cohorts and use smoking rates not from the time of death but from more than 20 years in the past [4,15,24]. In Korea, smoking rates have sharply decreased after 2000 compared to the 1980s and 1990s, suggesting that using smoking rates from recently established cohorts might underestimate the impact of smoking. This study employed 4 cohorts with different start years, highlighting the need to select a consistent point in time for smoking rates. Given the latency period between smoking and the onset of disease, some argue that a 10-year lag time is appropriate [25]. Furthermore, it has been reported that the contribution of smoking to the incidence of lung cancer and overall mortality is most fully seen after an average of 30 years [2,26]. Therefore, this study utilized the smoking prevalence from 1995, which is the closest year to 30 years before 2020, to ensure a representative measure of smoking rates.

According to the most recent findings reported by Jung et al. [15], the SAM in 2012 was 58 155 for all-cause deaths (49 704 in men and 8451 in women) and 20 581 for all cancers (19 184 in men and 1397 in women). These numbers were lower than the estimates in our study. Regarding specific diseases, in men, the SAM was notably higher for lung cancer (8881 deaths), stroke (3563 deaths), and IHD (3256 deaths). In women, the respective numbers were 887, 585, and 602. Given that our study shares similarities with that of Jung et al. [15], including the disease categories and methods, it can be inferred that SAM increased after 2013. This increase is likely attributable to a growing annual number of deaths, despite the lower PAF estimates in our study. Thus, a larger population exposed to the effects of smoking likely contributed to an increase in smoking-related deaths.

This study is not without limitations. The primary limitation is the reliance on self-reported smoking status, which might have resulted in underreporting of current smoking among women due to socio-cultural factors [27] or the misclassification of smoking status. Second, we did not account for smoking history at the time of enrollment, including smoking frequency, quantity, and duration. Third, we did not consider cessation among current smokers or resumption among former smokers, which could potentially affect HRs. Smoking cessation reduces the risks of cancer and cardiovascular diseases [28,29], while resuming smoking increases the risk of cancer [30]. Given the diversity of individuals' smoking behaviors, future studies should consider these characteristics. Fourth, additional confounding factors may influence the mortality risk associated with smoking-related diseases. However, adjustments for health behaviors or demographic characteristics do not significantly impact the estimates of mortality risk or SAM associated with these diseases [31,32].

In conclusion, this study conducted a meta-analysis of the risk of death from smoking-related diseases using data from 4 large Korean cohorts, with PAF and SAM values calculated for 2020. The PAF data indicated that smoking contributed to 33.2% of all-cause men deaths and 4.6% of all-cause women deaths. Regarding SAM, an estimated total of 60 213 deaths (53 930 in men and 6283 in women) due to smoking was projected for 2020, highlighting smoking as a significant public health issue. Given the historically high smoking prevalence in Korea, despite the current gradual decline, the harmful effects of smoking are likely to persist, with SAM expected to rise. To address these concerns, ongoing monitoring and prioritization of tobacco control and harm prevention policies are essential.

NOTES

Supplemental Materials

Supplemental materials are available at https://doi.org/10.3961/jpmph.23.471.

Conflict of Interest

The authors have no conflicts of interest associated with the material presented in this paper.

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