告されており、非侵襲的な測定手法に関しての精度と限界についての議論がなされている(4)。(なお、HEM-9000AI における中心血圧等の推定に関しては、2007 年の Takazawa らの報告が元となっている(5)。オムロンヘルスケア資料より。)

続いて、動脈硬化性病変を伴う各種疾患と中心血圧の関係についての報告がなされるようになり、2000 年には AI と I 型糖尿病の関係が(6)、2002 年には中心血圧（脈圧）と脂質代謝異常症患者の関係が報告されている(7)。また、2003 年には中心血圧と慢性関節リウマチ(8)、2006 年にはベーチェット病と AI(9)、2009 年には歯周病(10)との関係について、2010 年に脳微小血管疾患との関連についての報告がなされている(11)。2001 年には腎不全患者の予後について、AI との関係が検討されている(12)。

また、Pressure amplification (末梢血圧の脈圧と中心血圧の脈圧の比)に着目し、末梢血圧の予測能の年齢層による違いを指摘した報告(13)、80 歳以上の高齢者において脈圧の amplification が小さい者ほど心血管疾患を合併している割合が高いことも報告されている(14)。

続いて、報告の主流となるのが、薬剤等に対する末梢血圧と中心血圧の反応の差異についてである。2003 年のカフェインに対する中心血圧の上昇に関する報告(15)、2006 年には Atenolol と Eprosartan の中心血圧に対する作用の差異に関する報告(16)等がなされている。これらの動向に対応する形で、2007 年に Consensus Document が取りまとめられた(17)。その後も、Atenolol と Nebivolol について報告がなされており(18)、Perindopril・Atenolol ・Lercanidipine 及び Bendrofluazide それぞれの薬剤の各血圧指標に対する降圧効果についての比較した報告もなされている(19)。

さらに、夜間高血圧患者に対して、中心血圧と 24 時間血圧測定を併用する事が有用であるとの報告もなされ(20)、別の報告では、中心血圧は左室肥大を CAVI（Cardio-Ankle Vascular Index）は左室機能不全と関連するとの報告もある(21)。

<u>③大規模研究に関連する文献の紹介</u>

・The Anglo-Cardiff Collaborative Trial (2005)：地域住民 4,001 人を対象とした研究。若年の者においては、AI は直線的に増加するが、高齢者では平坦化する。逆に、PWV (Pulse Wave Velocity) は高齢者で直線的に増加を認めるが、若年者ではより平坦であった(22)。

・ASCOT-CAFÉ study（2006）：高血圧患者を対象とした治療効果を比較した研究。解析対象者は 2,073 人。良好な予後が得られたアムロジピンベース治療群で中心血圧が低かったことより、冠血管疾患の発生の差を明らかとしていると考えられた(23)。(スタチンについて解析した関連する研究も報告されている(24)。)

・The strong heart study（2007）：アメリカで実施された縦断研究。解析対象者は 2,403 人。循環器系疾患の発症と収縮期血圧、脈圧、中心血圧（収縮期及び脈圧）のいずれもが有意な関連がみられたが、もっとも強力な関連が認められたのは中心血圧の脈圧であった（ハザード比は、収縮期血圧：1.08 (1.02–1.14)、脈圧：1.10 (1.03–1.18)、中心血圧（収縮期）：1.07 (1.01–1.14)、中心血圧(脈圧)：1.15 (1.07–1.24)）(25)。

・The Anglo-Cardiff Collaborative Trial II (2008)：解析対象者は 10,613 人。上腕血圧の結果に基づき層化し、それぞれの層の中心血圧値を比較すると、多く重なっており、中心血圧の結果に基づいて判断する必要性が示唆された(26)。

D．考察

中心血圧に関して、非侵襲的な検査手法が実用可能となって以降、研究及び報告がなされてきた。この傾向は、非侵襲的に中心血圧が測定可能となったこと(SphygmoCor [AtCor Medical, Sydney, Australia]等の発売)、自動で測定が可能となったこと(HEM-9000AI(Omron Healthcare, Kyoto, Japan)の発売)等が関連していることが考えられる。

動脈硬化性病変を伴う各種疾患に関連して、網羅的に中心血圧等の状況について検討がなされている状況にある。

現在、薬剤への上腕血圧と中心血圧の反応の差異と死亡・循環器系疾患の発生の関連、中心血圧と長期予後の関連についての検討が活発になされている傾向にある。
Clinicaltrial.gov（http://clinicaltrial.gov/）、UMIN-CTR（http://www.umin.ac.jp/ctr/index-j.htm）に現在登録されている研究についてもこの傾向は認められる。

E．結論

中心血圧に関連し、新たな技術の開発により急速に研究が進んでいる現状が明らかとなった。

文献的検討を実施する事を通じ、研究の趨勢を見極める事により、効率的な研究の実施が可能となることが期待される。

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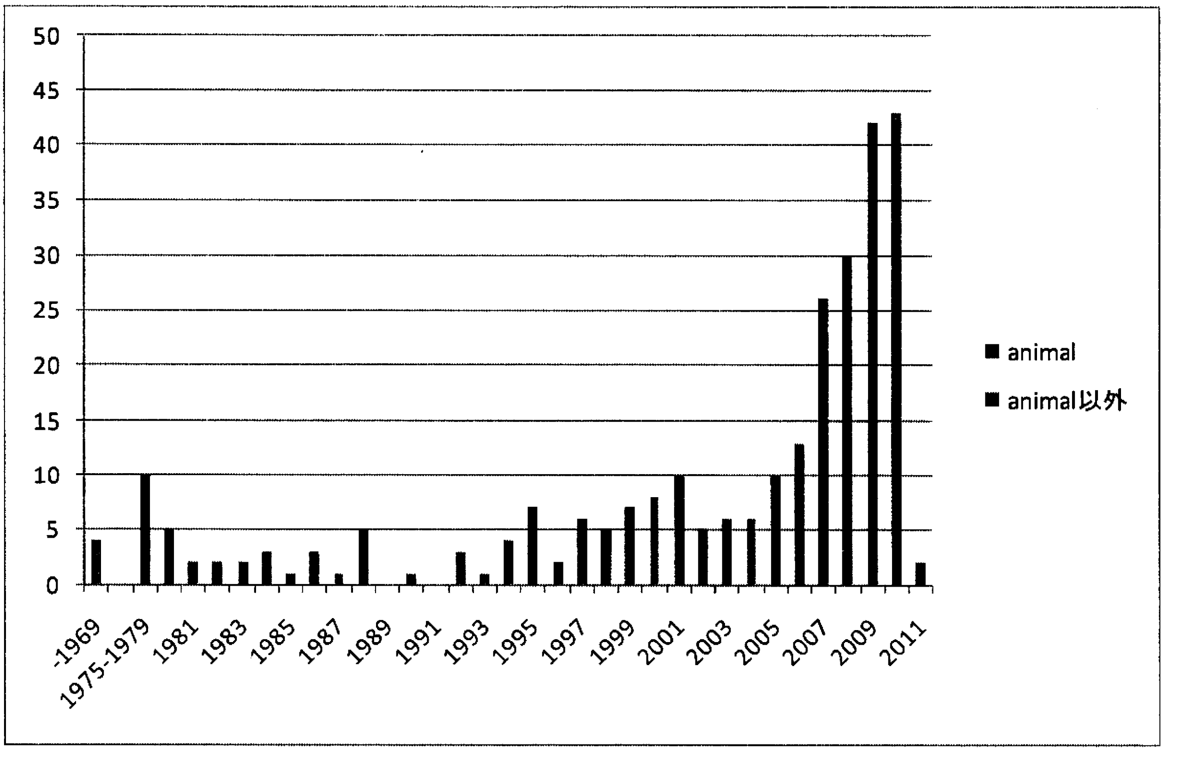
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Ⅲ. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

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Population attributable numbers and fractions of deaths due to smoking: A pooled analysis of 180,000 Japanese

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ABSTRACT

Objective. Age- and sex-specific population attributable fraction (PAF) and premature deaths attributable to smoking were estimated from a pooled analysis of cohort studies in Japan.

Methods. A pooled analysis of individual participant data from 13 well-qualified cohort studies throughout Japan (a total of 183,251 Japanese aged 40–89, 69,502 men and 113,749 women; the baseline years between 1987 and 1995 with average 10 years of follow-up) was performed. Poison regression model was used to estimate age- and sex-specific hazard ratios, and their PAFs of all-cause deaths and number of annual premature deaths attributable to smoking were estimated.

Results. Overall PAF attributable to smoking was 24.6% in men and 6.0% in women. The estimated number of annual premature deaths due to smoking was 121,854 (men: 109,998; women: 11,856) in Japan. The age-specific PAF was largest in men aged 60–69 (47.7%) and in women aged 50–59 (12.2%). In the older group aged 70–79 and 80–89, PAF was 15.4% and 8.0% in men and 3.5% and 1.5% in women, respectively.

Conclusions. Age-specific PAFs attributable to smoking in Japanese men are much larger than that reported from other Asian countries.

Introduction

Cigarette smoking is one of the most important, established risk factors for diseases that threaten human life (Peto et al., 1999). A large volume of evidence on the harm of smoking has been published (Ezzati and Lopez, 2003; Lopez et al., 2006), with challenges and programs to stop smoking being common in Western countries. The mortality attributable to smoking showed the substantial impact that smoking may have on people's health and has been reported from various countries (Centers for Disease Control and Prevention (CDC), 2008; Gu et al., 2009; Hara et al., 2002; Honjo et al., 2010; Hozawa et al., 2004; Katanoda et al., 2008; Peto et al., 2006; Peto et al., 1992; Pham et al., 2007). However, smoking rates still remain high in Asian countries (Martiniuk et al., 2006) and incentive measures for smoking cessation are urgently required.

A recent study from China reported the number of deaths attributable to smoking (Gu et al., 2009). We expect that the impact of smoking on total mortality may be different in Japan; a more economically developed Asian country with the highest life expectancy in the world (World Health Organization, 2005) but with a high smoking rate in men. Moreover, few studies from Asia have performed age- and sex-specific investigations on the contribution of smoking to mortality, as such investigations need large-scale data from cohort studies.

In this pooled analysis of 180,000 Japanese men and women from 13 well-qualified cohort studies in Japan, we examined age- and sex-specific population attributable fraction (PAF) of mortality by smoking and the annual number of premature deaths attributable to smoking.

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Methods

Study participants

The EPOCH-JAPAN (Evidences for Cardiovascular Prevention from Observational Cohorts in Japan) is the pooling project of a number of well-qualified cohort studies which investigates the relationship between health examination measures (laboratory measures and lifestyle factors) and mortality in the Japanese population. The EPOCH-JAPAN consists of 13 cohort studies in Japan and includes a total number of 188,321 participants followed up for an average of 10 years. The year range of baseline survey in the cohort was between 1987 and 1995. The details of this project have been described previously (Murakami et al., 2008). In the EPOCH-JAPAN database, the age range of the participants at study entry was set between 40 and 89 years and the termination of the follow-up was fixed at age 90. A total of 5070 participants were excluded from the analysis; missing information of variables (smoking habit, 4984; blood pressure, 74), few participants within a sparse age and sex strata in the cohort ($n = 12$). Finally, data for 183,251 participants were included in the analyses.

Hazard ratio estimation

We estimated age- and sex-specific hazard ratios for total mortality according to smoking habits. The statistical model was applied to each age group stratified by decades (40–49, 50–59, 60–69, 70–79, 80–89). Smoking habit was classified as either never smoked, former smokers or current smokers, with the group who had never smoked acting as the reference level. A Poisson regression model was used with adjustment for systolic blood pressure, body mass index, drinking status (drinkers/ex-drinkers/non-drinkers) and study cohort. To examine graded increases in the hazard ratios in the smoking categories, a score (1, 2, or 3) was assigned to each category and the statistical significance of increases in this score examined using the trend test.

Impact of smoking on the total deaths in Japan

The age- and sex-specific PAF (Hanley, 2001; Kleinbaum et al., 1982) for smoking was calculated by multiplying the estimated hazard ratio with the prevalence of smoking status among the Japanese population. We used the current age- and sex-specific smoking prevalence from the National Health and Nutrition Survey in Japan, 2006 (Ministry of Health Labour and Welfare, 2009). The estimated annual number of premature deaths due to smoking in the Japanese population was estimated from above PAFs. We used the age- and sex-specific number of all-cause deaths in the year 2008 (Japan Health and Welfare Statistics Association, 2005), with the corresponding PAFs multiplied by the total number of deaths to calculate the number of premature deaths in each category.

All statistical analysis was performed using SAS release 9.13 (SAS Institute Inc., Cary, NC, USA).

Results

Table 1 shows the baseline characteristics of the participants in this study. The total number of participants in this analysis was 183,251 (69,502 men and 113,749 women) and the total number of all-cause deaths was 17,224 (9612 men and 7612 women) during follow-up. The mean age at study entry was 59.6 years for men and 58.4 years for women and the mean follow-up period was 9.6 years for men and 9.9 years for women. As reported previously, the distribution of baseline characteristics was not different between the cohorts (Murakami et al., 2008).

Table 2 shows the age- and sex-specific mortality rates, hazard ratios and PAFs for all-cause deaths according to smoking status. Crude mortality rate was generally the highest in current smokers of the three smoking categories in each age and sex group. A significant graded increasing trend in multivariate-adjusted hazard ratios according to smoking status was observed in all age and sex groups, except for men and women aged 40–49. The adjusted hazard ratio in current smokers was highest in men aged 60–69 (hazard ratio 1.96) and women aged 50–59 (hazard ratio 2.21) compared with people who had never smoked. The PAF for smoking was consistently larger in current smokers than in former smokers. In men, the PAF in current smokers was largest in men aged 60–69 (33.4%), and for men aged 40–49 and 50–59 was more than 25%. In women, the PAF was largest in women aged 50–59 (11.1%).

Table 3 shows the PAF for smokers (former and current smokers combined) in each age and sex group and the estimated numbers of premature deaths attributable to smoking in Japan in 2008. The PAFs by age groups ranged from 8.0% (age 80–89) to 47.7% (age 60–69) in men and from 1.5% (age 80–89) to 12.2% (age 50–59) in women. Overall PAF in participants aged 40–89 was 24.6% in men and 6.0% in women. A total of 109,998 men and 11,856 women were estimated to have died attributable to smoking in Japan in 2008. These numbers were greatest in men aged 60–69 (45,409 deaths per year) and aged 70–79 (27,259 deaths per year).

Discussion

This large-scale pooled analysis of 180,000 Japanese from 13 well-qualified cohort studies showed that estimated annual premature deaths attributable to smoking habits were 110,000 for men and 12,000 for women in Japan. The proportion of premature all-cause deaths was 24.6% for men, with this proportion reaching 47.7% in men aged 60–69. This considerable loss of health attributable to smoking was confirmed in this analysis in Japan, a developed country with the greatest longevity in the world, but with a high smoking rate, especially in men.

The comprehensive global assessments of premature deaths attributable to smoking had been taken among developed countries (Peto et al., 1992). This report is the only one that we can find sex- and age-specific PAFs of developed countries. The report was focused on the global assessment of smoking harm so that the age group only divided into two categories (age from 35 to 69/age 70 and over). The updated report in year 2006 (Peto et al., 2006) showed that PAFs due to smoking in the developed countries are 30% (men aged 35–69), 19% (men age 70 and over), 11% (women aged 35–69) and 8% (women age 70 and over), respectively. Compared with our result, these numbers were lower in men and higher in women. In the country specific section in this report, they showed that the annual number of premature deaths due to smoking in Japan, year 2000 was estimated 90,000 in men and 24,000 in women, which were also lower in men and higher in women compared with our results. Particularly, this discrepancy is quite obvious in women aged 70 and over, where 20,000 in Peto et al. and 6000 in our study. We found that their smoking prevalence estimated from their method was quite different from the current smoking prevalence in Japanese women. We believe that our direct approach is more appropriate to show the current status of premature deaths due to smoking in Japan.

There have been several reports on PAF due to smoking in Asian countries including Japan (Hara et al., 2002; Hozawa et al., 2004; Katanoda et al., 2008; Pham et al., 2007). A report from north-east Japan (Miyagi) showed a larger PAF (34%) for men (Hozawa et al., 2004), whereas a report from southern Japan (Fukuoka) showed a smaller PAF (16.0%) (Pham et al., 2007). The PAFs reported from other nationwide cohort studies in Japan were similar to our results (Hara et al., 2002; Katanoda et al., 2008). For women, previously reported PAFs ranged from 4% to 8% in Japan (Hara et al., 2002; Hozawa et al., 2004; Katanoda et al., 2008; Pham et al., 2007) and our results come in the middle (6.0%). One reason for these variations in PAF may be the difference in hazard ratios of current smokers (ranged from 1.30 to 1.72), and it is important to note that the hazard ratio of current smokers played a dominant role in determination of PAF values in previous Japanese studies.

Although there have been only a few studies on PAF due to smoking in other Asian countries, a large-scale study was recently conducted in China (Gu et al., 2009). That study showed that overall

Table 1
Baseline characteristics of the study participants in each cohort (EPOCH-JAPAN).

Men

Cohort name	Geographic location (Prefecture)	Year of baseline survey	Follow up periods (years)		Number of participants	Age at study entry (years)		Blood pressure (mm Hg)				Smoking* status				Drinking† status				BMI (kg/m^2)		Number of all-cause mortality
								Systolic		Diastolic												
			Average	SD		Average	SD	Average	SD	Average	SD	Never	Past	Current	%	Never	Past	Current	Missing	Average	SD	
Tanno-Sobetsu	Hokkaido	1977	19	4	750	51	7	131	19	82	10	228	0	522	70	214	0	533	3	23.1	2.7	88
Osaki	Miyagi	1994	6	1	6,597	63	10	133	17	80	11	1,413	1,996	3,188	48	1,016	535	4,936	110	23.6	2.9	509
Ohasama	Iwate	1987	10	3	1,122	61	11	135	17	76	11	585	0	537	48	459	0	663	0	23.1	2.8	250
Oyabe	Ishikawa	1988	10	2	1,509	61	10	131	20	79	11	689	0	820	54	392	416	701	0	22.6	2.7	270
YKK workers	Toyama	1990	11	2	3,177	51	6	121	15	74	12	809	494	1,874	59	562	38	2,577	0	22.6	2.6	73
SPMI cohort	Shiga	1989–1991	9	3	1,937	54	8	133	18	82	11	544	229	1,164	60	398	0	1,528	11	22.6	2.7	149
Suita	Osaka	1989	6	2	2,300	60	11	131	21	80	12	423	772	1,105	48	504	99	1,694	3	22.7	2.9	164
RERF cohort	Hiroshima	1986	14	5	1,329	58	12	134	21	85	12	191	417	721	54	200	86	959	84	22.2	2.9	495
Hisayama	Fukuoka	1988	10	3	1,113	58	12	135	20	81	11	228	329	556	50	369	70	673	1	22.8	3.0	180
JACC study	Nationwide‡	1988–1990	9	2	10,621	58	10	135	19	81	11	2,392	2,639	5,590	53	2,020	547	7,811	243	22.8	2.9	1,342
NIPPON DATA80	Nationwide‡	1980	16	5	3,155	56	11	142	22	85	12	578	655	1,922	61	656	219	2,275	5	22.5	2.9	992
NIPPON DATA90	Nationwide‡	1990	9	2	2,759	58	12	140	20	85	12	605	708	1,446	52	962	206	1,591	0	23.0	3.0	412
Ibaraki	Ibaraki	1993	10	2	33,133	61	10	137	18	81	11	7,376	9,190	16,567	50	9,629	2,039	21,465	0	23.3	3.0	4,688
Total			10	3	69,502	60	10	135	19	81	11	16,061	17,429	36,012	52	17,381	4,255	47,406	460	23.1	2.9	9,612

Women

Cohort name	Geographic location (Prefecture)	Follow up periods (years)		Number of participants	Age at study entry (years)		Blood pressure (mm Hg)				Smoking* status				Drinking† status				BMI (kg/m^2)		Number of all-cause mortality
							Systolic		Diastolic												
		Average	SD		Average	SD	Average	SD	Average	SD	Never	Past	Current	%	Never	Past	Current	Missing	Average	SD	
Tanno-Sobetsu	Hokkaido	19	4	865	50	7	133	20	82	10	800	0	65	8	788	0	76	1	24.2	3.4	63
Osaki	Miyagi	6	2	7,181	62	9	130	18	78	11	6,706	120	355	5	5,209	196	1,407	369	24.1	3.2	225
Ohasama	Iwate	11	2	1,678	60	10	130	17	73	11	1,639	0	39	2	1,584	0	94	0	24.0	3.3	194
Oyabe	Ishikawa	10	1	3,208	58	10	126	20	75	11	3,126	0	82	3	2,770	399	39	0	23.2	3.1	255
YKK workers	Toyama	11	2	1,724	50	6	115	15	70	11	1,693	9	22	1	1,320	7	397	0	22.0	2.9	18
SPMI cohort	Shiga	9	3	2,568	54	8	132	17	79	10	2,467	14	87	3	2,048	0	514	6	23.0	3.0	63
Suita	Osaka	6	2	2,539	58	11	128	22	77	12	2,173	87	279	11	1,711	39	771	18	22.5	3.2	83
RERF cohort	Hiroshima	15	4	2,994	63	12	134	23	81	12	2,602	96	296	10	1,604	47	949	394	22.9	3.7	814
Hisayama	Fukuoka	11	3	1,518	60	12	133	22	76	11	1,382	31	105	7	1,366	17	133	2	22.9	3.3	123
JACC study	Nationwide ‡	10	2	17,853	57	10	132	19	78	11	16,989	208	656	4	14,143	195	3,273	242	23.3	3.2	913
NIPPON DATA80	Nationwide ‡	17	4	4,016	56	11	139	22	82	12	3,573	91	352	9	3,235	59	716	6	23.1	3.4	787
NIPPON DATA90	Nationwide ‡	10	2	3,697	58	12	138	20	81	12	3,284	87	326	9	3,443	35	219	0	23.1	3.3	312
Ibaraki	Ibaraki	10	2	63,908	59	10	132	18	78	11	60,357	462	3,089	5	57,784	125	5,999	0	23.6	3.2	3,762
Total		10	3	113,749	58	10	132	19	78	11	106,791	1,205	5,753	5	97,005	1,119	14,587	1,038	23.5	3.3	7,612

*Smoking status of ex-smokers was classified as never smokers in three cohort studies (Tanno-Sobetsu, Ohasama and Oyabe).
†Drinking status of ex-drinkers was classified as never drinkers in three cohort studies (Tanno-Sobetsu, Ohasama and Oyabe).
‡Study participants of the nationwide cohort study were selected from all areas of Japan.

Table 2
Age- and sex-specific mortality rates, adjusted hazard ratios and population attributable fractions of all-cause deaths according to smoking status (EPOCH-JAPAN).

Age groups (years)	Smoking status	Prevalence of smoking (%)‡	Person years of follow-up	Number of deaths	Crude mortality rate*	Adjusted hazard ratio†	95% Confidence interval	P for trend	PAF‡ (%)
Men									
40–49	Never	31.9	16,716	20	120	1.00			–
	Former	21.6	13,003	24	185	1.55	0.94 - 2.58		11.9
	Current	46.5	45,722	91	199	1.59	1.05 - 2.41	0.08	27.4
50–59	Never	28.9	39,736	105	264	1.00			–
	Former	24.9	30,583	95	311	1.16	0.91 - 1.47		4.0
	Current	46.2	90,304	396	439	1.64	1.36 - 1.97	<0.01	29.6
60–69	Never	39.2	51,521	285	553	1.00			–
	Former	26.0	52,616	471	895	1.55	1.36 - 1.76		14.3
	Current	34.8	118,131	1,350	1,143	1.96	1.76 - 2.19	<0.01	33.4
70–79	Never	51.7	36,982	695	1,879	1.00			–
	Former	28.4	53,893	1,190	2,208	1.17	1.08 - 1.27		4.8
	Current	19.9	81,197	2,422	2,983	1.53	1.42 - 1.65	<0.01	10.5
80–89	Never	51.7	10,511	620	5,899	1.00			–
	Former	28.4	12,238	749	6,120	1.07	0.97 - 1.17		2.0
	Current	19.9	13,795	1,099	7,967	1.30	1.20 - 1.42	<0.01	6.0
Overall	Never	38.4	155,466	1,725	1,110	1.00			–
	Former	25.5	162,333	2,529	1,558	1.20	1.26 - 1.14		5.1
	Current	36.2	349,149	5,358	1,535	1.54	1.62 - 1.47	<0.01	19.5
Women									
40–49	Never	81.4	126,961	117	92	1.00			–
	Former	4.8	1,557	2	128	1.52	0.46 - 4.95		2.5
	Current	13.8	9,624	9	94	0.95	0.53 - 1.71	0.96	−0.7
50–59	Never	86.8	278,258	455	164	1.00			–
	Former	4.0	2,371	5	211	1.26	0.60 - 2.65		1.0
	Current	9.2	17,193	62	361	2.21	1.75 - 2.80	<0.01	11.1
60–69	Never	91.1	351,145	1,338	381	1.00			–
	Former	2.6	3,368	22	653	1.64	1.14 - 2.34		1.6
	Current	6.4	15,547	100	643	1.70	1.42 - 2.03	<0.01	4.5
70–79	Never	94.8	247,653	2,710	1,094	1.00			–
	Former	2.4	3,201	63	1,968	1.59	1.28 - 1.98		1.4
	Current	2.8	10,973	222	2,023	1.74	1.54 - 1.96	<0.01	2.1
80–89	Never	94.8	55,577	2,264	4,074	1.00			–
	Former	2.4	1,003	54	5,384	1.16	0.92 - 1.47		0.4
	Current	2.8	3,109	189	6,079	1.39	1.22 - 1.59	<0.01	1.1
Overall	Never	89.2	1,059,594	6,884	650	1.00			–
	Former	3.3	11,500	146	1,270	1.39	1.61 - 1.21		1.3
	Current	7.5	56,446	582	1,031	1.63	1.75 - 1.51	<0.01	4.7

PAF, population attributable fraction.
*Rates per 100,000 person-years.
†A Poisson regression model was used to estimate hazard ratios adjusted for potential confoundings (systolic blood pressure, body mass index, drinking status and study cohort).
‡Each PAF of the former and current smokers showed the partial component of PAF in sex and age category. These PAFs were estimated from the hazard ratios of our study and the age- and sex-specific smoking prevalence from the National Health and Nurition Survey in Japan, 2008.

PAF of all-cause deaths due to smoking was 12.9% in men, which is considerably smaller than the value measured in our study, despite the smoking rate being rather higher in China (71.1% in men). Age-specific PAFs were also reported in that study and were also smaller than those calculated in our study. For example, the PAF in men aged 40–54 was 12.7% in China, less than half the PAF values measured in our study (39.3% for ages 40–49; 33.6% for ages 50–59). One possibility of this difference comes from the study period that studies were conducted. The baseline survey in the China study began at 1991 and the follow-up ended in 2000, although some of our cohorts started before 1990. In our study, the baseline survey of three cohorts were conducted before mid-1980s and their proportion among the study participants are 8% ($n = 5234$) in men and 7% ($n = 7875$) in women. We think the difference of the study period dose not totally explain PAF difference in Japan and China. These lower PAF values in China may be explained by the smaller hazard ratio (HR = 1.21) in male smokers (current and former combined), compared with hazard ratios of 1.54 in current smokers and 1.20 in former smokers measured in our study. All-cause mortality rate in people who had never smoked were also different between the two studies; 1279 per

Table 3
Age- and sex-specific population attributable fraction for all-cause deaths due to smoking in EPOCH-JAPAN and the estimated premature deaths due to smoking in Japan, 2008.

Age groups (years)	Population attributable fraction (%)*		Number of all-cause deaths in 2008, Japan†		Estimated premature deaths due to smoking	
	Men	Women	Men	Women	Men	Women
40–49	39.3	1.8	16,851	8,511	6,624	152
50–59	33.6	12.2	52,812	24,629	17,718	2,995
60–69	47.7	6.1	95,137	42,409	45,409	2,591
70–79	15.4	3.5	177,349	99,248	27,259	3,444
80–89	8.0	1.5	163,266	181,883	12,988	2,674
Overall	24.6	6.0	505,415	356,680	109,998	11,856

*Sum of population attributable fractions for former smokers and current smokers.
†Number of deaths in 2008 in Japan was obtained from the Vital Statistics of Japan, 2008.

100,000 person-years for men in the Chinese study, which was higher than that in our study (1110 per 10,0000 person-years). This higher background mortality rate, which is the denominator of hazard ratio, leads to smaller PAFs attributable to smoking in China. It would be expected that background mortality rate of Chinese non-smokers will decrease and the relative amounts of smoking-related causes of deaths (cancer and cardiovascular diseases) will increase in the future, like contemporary situation in Japan. Our results from Japan may become more common feature of health threat in Asian countries caused by smoking.

Age-specific analysis of PAF provided a clear picture of smoking harm. This harm persisted through the age categories and also substantially observed in people aged 70 and over in the Japanese population. A cohort study in an elderly population in Hong Kong also showed that the PAF for smoking in people aged 65 and over was 23.4% for men and 4.8% for women (Lam et al., 2007a, 2007b). Our findings in elderly people provide evidence that harm from smoking has a broad impact from young age to older age in developed Asian regions. The PAF for smoking in people aged 80–89 was only available in countries with longer life spans such as Japan, with our study being the only one in the Asian region able to estimate this figure.

The relatively high PAF among men aged 60–69 could partly be explained by the cohort effect. The baseline survey year of the cohort of EPOCH-JAPAN ranged from 1987 to 1995. This shows that the men aged in the 60–69 year in our study correspond to the generation who spent their 20s just after Japan defeated World War II. At that time, the smoking habit spread among Japanese men and the amount of lifetime smoking of age 60–69 in our study would be large compared to other age groups.

This study had several limitations. First, we only have all-cause death and a disease specific mortality was not available from the database. Second, the quantity of cigarettes smoking was not examined in our study. Only few cohorts collected the amount of smoking and every cohort used slightly different type of smoking category. To integrate several type of smoking classification of the 13 cohort studies into one, we finally set the smoking category as follows; never, former and current. Third, information of smoking status in the participants is based on the baseline survey of each cohort and changes in smoking status during follow-up were not considered in our study. As the smoking rate in Japanese men has been decreasing constantly, these misclassifications of smoking status during the follow-up may underestimate the relationships. Fourth, we focused mainly on individual smoking habits and did not take into account the effect of environmental tobacco smoke. Prior to 2000, smoking was not restricted in public places and environmental tobacco smoke was common in work places and homes in Japan. Passive smoking has been reported to increase mortality of non-smokers (Kurahashi et al., 2008; McGhee et al., 2005), although we were unable to estimate this impact in this pooled analysis.

Using the data of this pooled analysis, we estimate that approximately 110,000 men and 12,000 women die every year due to smoking in Japan. This number of deaths corresponds to 36% of annual deaths from cardiovascular diseases and lung cancer in Japan (364,547 deaths in year 2006) (Japan Health and Welfare Statistics Association, 2005). These large numbers therefore have a major impact on public health policy and the Japanese nation. Even though Japan accepted the WHO Framework Convention on Tobacco Control (FCTC) in June 2004, the smoking rate in Japan still remains high compared with Western countries. The Health Promotion Act was introduced in Japan in 2002. According to this law, smoking in public places was prohibited to protect non-smokers from passive smoking. In October 2010, the tobacco tax has drastically risen by the Japanese government and an urgent and an effective measure is now taken to accomplish lower smoking rate in the next decades. We believe the present study gives an important evidence to promote anti-smoking campaign to the policy makers in Japan. Our results also encourage promoting smoking ban campaign of other Asian countries with high smoking rates.

In conclusion, pooled data of 180,000 Japanese from well-qualified cohort studies in Japan revealed that there are a large number of deaths attributable to smoking in Japan and age-specific PAFs attributable to smoking in men are much larger than that reported from China.

Conflict of interest statement

No conflict of interest.

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