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Abstract

Background: Smoking is a known risk factor for cardiovascular morbidity and mortality, but several Korean studies have shown differing results on the association of current smoking status and the risk of cardiovascular disease (CVD). The aim of the present study was to investigate the association between smoking status and CVD (myocardial infarction and stroke) using national representative population-based samples. The aim was also to investigate the effects of hidden smokers on the association between CVD and smoking.

Methods: Data were acquired from 28,620 participants (12,875 men and 15,745 women), age 19 years or older, who participated in the Korea National Health and Nutrition Examination

Survey (KNHANES) conducted from 2008 to 2016.

Results: The multivariable logistic regression analysis showed that ex-smoking status was correlated with CVD when self-reported (odds ratio [OR]: 1.62; 95% confidence interval [CI]: 1.20–2.19) and for survey-cotinine verified-smoking status (OR: 1.57; 95% CI: 1.20–2.19). Interestingly, the present study showed current smoking was not significantly associated with CVD. For the effect of sex on smoking and CVD, self-reported and survey-cotinine-verified ex-smoking status were correlated with CVD in males (OR: 1.45; 95% CI: 1.04–2.04 and OR: 1.43; 95% CI: 1.02–2.02) and in females (OR: 2.74; 95% CI: 1.59–4.71 and OR: 2.92; 95% CI: 1.64–5.18). The ratios of cotinine-verified to self-reported smoking rates were 1.95 for women and 1.08 for men.

Conclusions: In the current study, while ex-smoking status was significantly associated with CVD, current smoking status was not. Female ex-smoking status had a higher adjusted odds ratio for CVD than males compared to non-smoking status. An effect of hidden female smoking was also found on the association between smoking status and CVD in Korean adults.

Key words: smoking, myocardial infarction, stroke, hidden smoker

Introduction

Smoking is a known risk factor of cardiovascular morbidity and mortality [1]. However, while more than 4000 chemical substances contained in a cigarette are known to have adverse effects on various cardiovascular diseases (CVD) [2], the pathophysiological mechanisms underlying the association between smoking and CVD have not been fully elucidated.

The CHANCES consortium (Consortium on Health and Ageing: Network of Cohorts in Europe and the United States) study showed a strong relationship between tobacco smoking and CVD [3]. This study used data from 10 cohort studies that showed a cardiovascular mortality hazard ratio of 2.07 (95% confidence interval [CI]: 1.82–2.36) for current smokers and 1.37 (95% CI: 1.25–1.49) for former smokers compared to participants who had never smoked. Another meta-analysis study based on prospective studies showed that the relative

risk (RR) of sudden cardiac death due to CVD, including coronary heart disease and stroke, was 3.06 (95% CI: 2.46–3.82) for current smokers and 1.38 (95% CI: 1.20–1.60) for former smokers compared to participants who had never smoked [4].

Moreover, the INTERHEART study showed that current smoking status (odds ratio [OR] 2.87) was significantly associated with myocardial infarction (MI) [5], and a UK biobank study showed that the hazard ratios for MI were 3.46 (95% CI: 3.02–3.98) in female current smokers and 2.23 (2.03–2.44) in male current smokers [6]. One meta-analysis study showed that the pooled relative risk of stroke associated with current smoking status vs. non-smoking status was 1.67 (95% CI: 1.49–1.88) in men and 1.83 (95% CI: 1.58–2.12) in women [7].

However, several Korean studies showed contrasting results on the association between current smoking status and CVD risk in adults [8, 9]. A national study showed that smoking status was significantly associated with stroke (RR: 1.060, 95% CI: 1.022–1.100) but not MI (RR: 1.004, 95% CI: 0.958–1.051) [8]. In addition, another national study showed that, compared to a non-smoking group of Korean adult males, the ORs (95% CI) for physician-diagnosed stroke and MI in a current smoker group were 0.84 (0.74–0.94) and 0.96 (0.82–1.12), respectively, and 1.38 (1.24–1.53) and 1.45 (1.26–1.67), respectively, in a past smoker group [9].

Recently, a report showing that ratios of cotinine-verified to self-reported smoking rates were 2.36 for women and 1.12 for men in Korea [10]. In a previous report, an effect was found of hidden female smoking on the association between smoking and hypertension in Korean adults [11]. It is currently proposed that contradictory results from other countries may be due to hidden female smokers.

Therefore, the first aim of the study was to investigate the association between smoking status and cardiovascular disease using different nationally representative population-based samples. The second aim was to investigate the effects of hidden female smokers on the association between cardiovascular disease and smoking in Korean adults.

Methods

Study population

This study was based on data obtained from the 2008–2016 KNHANES study. KNHANES, which was a cross-sectional survey designed to examine the health and nutritional status of the non-institutionalized Korean population.

Of the total 76,909 KNHANES participants, 48,289 participants were excluded due to the following criteria: under 18 years old, no smoking history, no MI information, no stroke information, no urine cotinine test, no history of renal failure information, or serum creatinine ≥ 1.5 mg/dL. The remaining 28,620 participants (12,875 men and 15,745 women) were included in the final analysis.

General characteristics, anthropometry, and laboratory tests

The contents of the questionnaire used in KNHANES included sex, age, marital status, employment status, education level, monthly family income, number of household members, residence area, and body mass index (BMI). The questionnaire also ascertained the presence of or history of hypertension, diabetes, MI, and stroke. The respondents' residential areas were categorized as urban (an administrative division of a city) or rural (not classified as an administrative division of a city). The definition of a city in Korea is a place where more than 50,000 people live. Monthly family income indicates monthly-equalized family income and was calculated by dividing the total family income by the square root of the number of household members. In KNHANES, monthly family income was classified into quartiles in order to determine the monthly household income level (1: low, 2: middle low, 3: middle high, and 4: high). Education level was defined as less than middle school, middle school, high school, and college or more. BMI was calculated as weight (kilograms) divided by height (meters squared) and was categorized into three groups: normal weight (< 23 kg/m^2), overweight (23–25 kg/m^2), and obese (≥ 25 kg/m^2) [12].

Cigarette smoking status was divided into three categories: smoker, ex-smoker, and never smoked. Respondents who reported having consumed ≥ 100 cigarettes in their lifetime or responded "yes" to the question, "Do you smoke cigarettes now?" were regarded as smokers.

Participants answering "no" to the same question were classified as ex-smokers. Respondents who consumed < 100 cigarettes in their lifetime were regarded as never having smoked.

Urinary cotinine was measured by tandem mass spectrometry with a tandem mass API 4000 (Applied Biosystems, Carlsbad, CA, USA) and by gas chromatography and mass spectrometry with a Perkin Elmer Clarus 600T (PerkinElmer, Turku, Finland). Respondents with urinary cotinine concentrations ≥ 50 ng/mL were considered cotinine-verified smokers, and those with cotinine levels < 50 ng/mL were cotinine-verified non-smokers [13].

To define MI and stroke, the following survey question was used in this study: "Have you ever been diagnosed with myocardial infarction or stroke by a physician?" For convenience, CVD to MI and stroke were limited. In a similar questionnaire, blood pressure (BP) measurements and medication history were used to define hypertension with the following question: "Have you ever been diagnosed with hypertension by a physician or take a medicine now?" Seated BP was measured using a standardized automated oscillometric device after a 5-min rest period. If BP was abnormally high or low, BP was reassessed with a mercury sphygmomanometer by a trained nurse. Hypertension was defined as having elevated BP (systolic BP [SBP] ≥ 140 mmHg and/or diastolic BP [DBP] ≥ 90 mmHg). Participants currently prescribed anti-hypertensive medication were also considered to be hypertensive. Diabetes was defined as a fasting blood glucose (FBG) of 126 mg/dL. Participants who reported being diagnosed with diabetes by a physician and prescribed diabetes medication including insulin were also considered to be diabetic.

To better understand the link between MI, stroke, and smoking, a new variable was created for defining smoking status (SCS, survey-cotinine-verified smoking status) (Table 1). It was assumed that smoking in this variable included all smoking types, including light, intermittent, passive, hidden, and active heavy smoking (Table 1).

Statistical analysis

All statistical analyses was conducted using the Statistical Package for the Social Sciences (SPSS) complex sample procedures since KNHANES data were collected through a representative, stratified, and clustered sampling method. Values are presented as number of participants or estimates (95% CI). Data are expressed as the mean ± standard deviation (SD)

and as the median for continuous variables and as percentages (%) for categorical variables.

Calculations of crude odd ratios and 95% CI values for CVD in relation to potential risk factors were performed using univariable logistic regression models. Finally, multivariable logistic regression analysis was carried out to identify the relationships between risk factors and CVD to evaluate the relationship of self-reported and cotinine-verified smoking status with CVD. Sex, age, marital status, employment status, education level, monthly family income, number of household members, residence area, smoking status, BMI, presence of hypertension and presence of diabetes were corrected for in the final multivariable logistic regression model.

Statistical analysis was conducted using SPSS version 21.0 (SPSS Inc. Chicago, IL, US). For all analyses, p values were two-tailed, and a p value < 0.05 was considered statistically significant.

Results

Clinical characteristics

A total of 28,620 subjects from the KNHANES were included in this study. Mean age was 49.55 ± 16.35 years. Slightly over half (52.3%) were male. The majority of participants were married (75.0%), employed (64.2%), and had an education level of high school or higher (73.9%). Most subjects lived in urban areas (83.1%) (Table 2).

Smoking status

Self-reported smoking prevalence was 25.5%, whereas the prevalence of cotinine-verified smokers in the overall population was 29.7% (Table 2). Cotinine-verified smoking prevalence for men and women was 43.3% (5,578/12,875) and 9.9% (1,559/15,745), respectively (Table 3). The overall prevalence of self-reported ex-smokers and current smokers was 18.1% and 25.5%, the percentages were 30.6% and 43.5% in men and 4.3% and 5.9% in women (Tables 2, 3). Of the 7,137 cotinine-verified male and female smokers, 813 (11.4%) were self-reported non-smokers and 517 (7.2%) were self-reported ex-smokers. Specifically, 2.3% and

7.3% of male cotinine-verified smokers were self-reported non-smokers and ex-smokers, respectively, whereas 43.7% and 7.1% of female cotinine-verified smokers were self-reported non-smokers and ex-smokers, respectively (Table 3). The ratios of cotinine-verified to self-reported smoking rates were 1.95 (1,559/801) for women and 1.08 (5,578/5,182) for men (Table 3).

Relationship between MI or stroke and smoking

In a univariate analysis, subjects with MI or stroke were prone to be male ($p < 0.01$), older ($p < 0.01$), single (separated or divorced) ($p < 0.01$), unemployed ($p < 0.01$), less educated ($p < 0.01$), obese ($p < 0.01$), have a lower monthly family income ($p < 0.01$), have fewer household members ($p < 0.01$), living in a rural setting ($p < 0.01$), have hypertension ($p < 0.01$), and have diabetes ($p < 0.01$) compared to subjects without CVD (Table 4). For self-reported smoking status, ex-smoking status was significantly correlated with CVD ($p < 0.01$), and for SCS, ex-smoking status was also correlated with CVD ($p < 0.01$). However, for all three types of smoking status, current smoking status was not significantly correlated with CVD using univariate statistical analysis ($p > 0.05$) (Table 4).

The multivariate logistic regression analysis showed that for self-reported smoking status, ex-smoking status was correlated with CVD (OR: 1.62; 95% CI: 1.20–2.19). Also, for SCS, ex-smoking status was correlated with CVD (OR: 1.57; 95% CI: 1.20–2.19) (Table 5).

To determine the effects of sex on smoking and CVD, sex differences were analyzed separately. For male participants, self-reported status and survey-cotinine-verified ex-smoking status were correlated with CVD (OR: 1.45; 95% CI: 1.04–2.04, OR: 1.43; 95% CI: 1.02–2.02). Female self-reported status and survey-cotinine-verified ex-smoking status were also correlated with CVD (OR: 2.74; 95% CI: 1.59–4.71, OR: 2.92; 95% CI: 1.64–5.18) (Tables 6, 7). Therefore, the current results indicate that sex affected the incidence of CVD in this study.

Discussion

The main findings of this study showed that, while ex-smoking status was significantly

associated with CVDs, current smoking status was not, and female ex-smoking status had higher adjusted OR for CVD than males compared to non-smoking status. In addition, there was an effect of hidden female smoking on the association between smoking status and CVD in Korean adults.

Smoking is an established risk factor for cardiovascular morbidity and mortality [1].

Cigarette smoke contains over 4000 compounds, many of which are extremely reactive and affect the physiology of several systems in the body. These compounds include nicotine, tar, carbon monoxide, and nitrogen oxide [14].

Nicotine can elevate BP via various biological mechanisms: sympathomimetic action, modulation of the renin angiotensin system, and acute vasopressor effects. All of these mechanisms are associated with increases in inflammatory markers through the upregulation of arginine vasopressin and endothelin-1 [15]. Nicotine can also increase low-density lipoprotein and decrease high-density lipoprotein, thereby accelerating the progression of atherosclerosis [2].

Carbon monoxide and hemoglobin combine to produce carboxy-hemoglobin, which induces hypoxia, increases in the number of red blood cells, and increases in blood viscosity, thereby, inducing thrombosis and atherosclerosis [16]. Through these mechanisms, structural damage to the arterial walls from smoking is believed to cause MI and induce stroke.

Previous studies have shown that current smoking status is significantly associated with MI [5, 6] and stroke [7, 17], but the present study has not shown a significant association. Proposed herein, is that the differing results may be due to differences in study design. The study design of the previous studies were case-control and population-based prospective cohorts; the present study design was cross-sectional. Other Korean and Polish studies that used cross-sectional designs showed similar results to the current study [8, 9, 18]. A Korean study using the 2009 Community Health Survey data gathered by the Korea Centers for Disease Control and Prevention showed current smoking was not associated with physician-diagnosed MI (OR: 0.96; 95% CI: 0.82–1.12) and stroke (OR: 0.84; 95% CI: 0.74–0.94), but ex-smoking was associated with physician-diagnosed myocardial infarction (OR: 1.45; 95% CI: 1.26–1.67) and stroke (OR: 1.38; 95% CI: 1.24–1.53) [9]. In the Polish study, the

researchers showed a significant association between former smokers and CVD (OR: 1.33; 95% CI: 1.05–1.68), but not between current smokers and CVD (OR: 1.06; 95% CI: 0.77–1.47) [18]. In addition, after cardiovascular events, patients were advised to quit smoking by physicians [19]. Therefore, the idea that cross-sectional studies, including the present study, might show no association between current smoking and CVD, but a significant association between ex-smoking and CVD.

For stroke, previous Korean studies showed different results. One study showed that ex-smoking status was associated with stroke in Korean male adults, but current smoking was not [9]. Another study showed that current smoking status was associated with stroke (OR: 1.060; 95% CI: 1.022–1.100) [8]. Because the prevalence of stroke increases with age, it was assumed these differing results may be due to differences in participant age. One study included male subjects 30 years or older [9], while another study included subjects 50 years or older [8]. In the current study, participants 19 years or older were included and showed that ex-smoking status, but not current smoking status, was associated with stroke.

In the present study, female ex-smoking status had higher odds ratio for CVD than males, compared to non-smoking status. Two hypotheses are herein proposed. First, the use of oral contraceptives and postmenopausal hormone replacement therapy in female smokers might increase CVD incidence, and the association between ex-smoker and CVD might be higher in female smokers due to smoking cessation after a CVD attack. The use of oral contraceptives and postmenopausal hormonal replacement therapy in smokers was known to increase the risk of MI and stroke [20–22]. Although the use of oral contraceptives did not increase the risk of MI in non-smokers, the use of oral contraceptives significantly increased the risk of MI in smokers [23]. The use of oral contraceptives also showed a higher prevalence of stroke in smokers compared to non-smokers [20], and the use of postmenopausal hormonal replacement therapy showed the same results for MI and stroke [21, 22]. Second, it was assumed these effects might be due to more female hidden smokers than males. In the case of self-reported ex-smokers, the probability of being identified as cotinine-verified smokers was 10.46% for men and 18.6% for women.

In the present study, the ratios of cotinine-verified to self-reported smoking rates were 1.95 for women and 1.08 for men. These rates were similar to the findings of a previous Korean

study [10]. That study reported that ratios of cotinine-verified to self-reported smoking rates were 2.36 for women and 1.12 for men [10], but studies in other countries reported no sex differences in underreporting the rate of smoking history [24, 25].

In a study from the United States, the rates of agreement between self-reported and cotinine-verified smokers were 91.6% for women and 89.7% for men [24]. Additionally, a study from Finland documented that 2.5% of men and 2.7% of women who self-reported as non-smokers had positive serum cotinine levels [25].

This result means there were more hidden female smokers than hidden male smokers in the current study. It was assumed that self-reported smoking in Korean women underestimates the true prevalence as a result of Confucianism. The adoption of Confucianism can result in a patriarchal culture in which female smoking is stigmatized [26]. The discrepancy in the underreporting rates between the sexes could lead to statistical inconsistencies.

To better understand the association between CVD and smoking, a new variable was created; SCS, in order to consider the effects of hidden smoking and other types of smoking. This new variable showed similar results compared to self-reported smoking status. Therefore, it isplausible to suggest that passive and light smoking may affect CVD development and are similar to affects of active smoking.

Light and social smokers often are not detected; many of these individuals have the perception of being non-smokers [27, 28]. However, a recent study reported that social smokers had significantly higher risks of CVD than non-smokers. Moreover, no significant differences in the development of hypertension have been reported between social smokers and current smokers [29]. Another report showed that light smoking was associated with a significantly higher risk of dying from ischemic heart disease [30]. With respect to the relationship between CVD and social and light smoking, a stable pattern of chronic low-level consumption may be assumed to have similar effects on CVD as constant, current active smoking.

Limitations of the study

There are several limitations to this study. First, because this study was based on a survey,

there may be selection and recall biases. Second, because this study was cross-sectional in design,   a causal relationship between smoking and CVD could not be confirmed. Third, although CVD was defined as MI and stroke in this study, CVD also includes other coronary heart diseases such as angina and peripheral arterial diseases; this was considered to be a limitation in the present study. Finally, potential confounding factors, including amount and duration of smoking, diet patterns, and genetic or sex variations affecting nicotine metabolism, still exist. Further prospective and collaborative worldwide studies are needed to clarify the effect of hidden female smoking on CVD. However, the strength of this study is its use of nationally and widely sampled data to assess sex-specific relationships between smoking status and CVD through the creation of a new variable, SCS. This new variable was used to evaluate the effect of hidden smoking on CVD.

Statement of ethics

This study was approved by the Institutional Review Board (IRB) of Samsung Changwon Hospital (IRB No: SCMC2019-04-005). Informed consent was waived by the board.

Conclusions

This large observational study found that ex-smoking status was associated with CVD and female ex-smoking status had a higher adjusted OR for CVD than males compared to non-smoking status. In addition, there was an effect of hidden female smoking on the association between smoking status and CVD in Korean adults.

Conflict of interest: None declared

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Table 1. Definition of survey-cotinine-verified smoking status (SCS).

Self-reported smoking status	Cotinine-verified smoking status	
	Non-smoker (≤ 50 ng/mL)	Smoker (> 50 ng/mL)
Non-smoker	Non-smoker (n = 16,595)	Smoker (n = 813)
Ex-smoker	Ex-smoker (n = 4712)	Smoker (n = 517)
Smoker	Smoker (n = 176)	Smoker (n = 5,807)

Table 2. Demographic characteristics of subjects.

Characteristics	Sample size	Estimate % (95% CI)
Sex (n = 28,620)		
Male	12,875	52.29 (51.74–52.85)
Female	15,745	47.71 (47.15–48.26)
Age (n = 28,620)		
< 50	14,332	62.00 (61.04–62.97)
50–59	5515	18.89 (18.27–19.51)
60–69	5000	11.30 (10.85–11.77)
≥ 70	3773	7.81 (7.41–8.24)
Marital status (n = 26,740)		
Married	20,644	74.95 (74.03–75.84)
Single (separated or divorced)	3491	10.10 (9.61–10.62)
Never-married	2605	14.95 (14.15–15.80)
Employment status (n = 28,541)		
Employed	17,307	64.19 (63.40–64.97)
Unemployed	11,234	35.81 (35.03–36.60)
Education level (n = 28,541)		
< High school	9918	26.10 (25.18–27.05)
High school	9755	38.94 (38.08–39.80)
> High school	8868	34.96 (33.89–36.04)
Monthly family income (n = 28,310)		
< 25th	5284	14.80 (14.06–15.57)
25–50th	7149	24.85 (23.96–25.76)
50–75th	7851	29.64 (28.68–30.61)
≥ 75th	8026	30.72 (29.40–32.06)
Number of household members (n = 28,608)		
1	2521	7.26 (6.68–7.88)
2	7695	21.58 (20.84–22.33)

14

3	6968	26.67 (25.82–27.54)
4	7725	30.92 (29.95–31.91)
≥ 5	3699	13.58 (12.80–14.39)
Residence area (n = 28,620)		
Urban	22,156	83.14 (81.04–85.05)
Rural	6104	16.86 (14.95–18.96)
Smoking status		
Self-reported 1 (n = 28,620)		
Non-smoker	17,408	56.41 (55.73–57.09)
Ex-smoker	5229	18.05 (17.55–18.56)
Smoker	5983	25.54 (24.87–26.22)
Cotinine-verified (n = 28,620)		
Non-smoker	21,483	70.33 (69.58–71.07)
Smoker	7137	29.67 (28.93–30.42)
Survey-cotinine verified (n = 28,620)		
Non-smoker	16,595	53.57 (52.85–54.29)
Ex-smoker	4712	15.98 (15.49–16.47)
Smoker	7313	30.45 (29.72–31.20)
Body mass index (n = 28,620)		
< 23	12,318	43.64 (42.90–44.37)
23–25	6812	23.71 (23.13–24.30)
≥ 25	9415	32.66 (31.95–33.37)
Hypertension (n = 28,620)	7917	23.69 (23.04–24.36)
Diabetes (n = 28,620)	3082	8.80 (8.42–9.20)
Myocardial infarct or stroke (n = 28,620)	811	1.98 (1.81–2.16)
Myocardial infarct	236	0.60 (0.51–0.70)
Stroke	599	1.44 (1.30–1.60)

Table 3. Self-reported and cotinine-verified smoking status in male and female participants.

Self-reported smoking status	Cotinine-verified smoking status (estimate % [95% CI])		
	Total	Non-smoker	Smoker
Male (n = 12,875)			
Total		53.4 (52.3–54.4)	46.6 (45.6–47.7)
Non-smoker	26.0 (25.0–26.9)	24.8 (23.9–25.7)	1.2 (1.0–1.4)
Ex-smoker	30.6 (29.6–31.5)	27.4 (26.5–28.3)	3.2 (2.9–3.6)
Smoker	43.5 (42.4–44.5)	1.2 (1.0–1.5)	42.3 (41.2–43.3)

Female (n = 15,745)

Total		88.9 (88.2–89.6)	11.1 (10.4–11.8)
Non-smoker	89.8 (89.1–90.4)	85.1 (84.3–85.9)	4.7 (4.2–5.2)
Ex-smoker	4.3 (4.0–4.8)	3.5 (3.2–3.9)	0.8 (0.7–1.0)
Smoker	5.9 (5.4–6.4)	0.3 (0.2–0.4)	5.6 (5.1–6.1)

Table 4. Crude odds ratios and 95% confidence intervals (CI) for myocardial infarction and stroke prevalence.

Characteristics	Odds ratio (95%CI)		
	Total	**Male**	**Female**
Sex			
Male	1.40 (1.19–1.65)	–	–
Female	Reference	–	–
Age			
< 50	Reference	Reference	Reference
50–59	8.10 (5.48–11.96)	7.65 (4.78–12.24)	11.07 (5.45–22.47)
60–69	21.90 (15.38–31.19)	21.03 (13.81–32.02)	31.48 (16.18–61.26)
≥ 70	33.92 (24.05–47.85)	28.01 (18.40–42.64)	63.78 (33.44–121.65)
Marital status			
Married	Reference	Reference	Reference
Single (separated or divorced)	2.28 (1.87–2.80)	1.94 (1.30–2.87)	3.48 (2.70–4.49)
Never-married	0.15 (0.08–0.29)	0.15 (0.07–0.31)	0.10 (0.02–0.40)
Employment status			
Employed	Reference	Reference	Reference
Unemployed	2.98 (2.50–3.55)	3.74 (2.99–4.68)	3.44 (2.61–4.55)
Education			
< High school	8.62 (6.45–11.50)	7.44 (5.33–10.39)	20.45 (10.76–38.86)
High school	1.90 (1.37–2.63)	1.83 (1.27–2.64)	2.62 (1.31–5.24)
> High school	Reference	Reference	Reference
Monthly family income			
< 25th	6.30 (4.78–8.30)	5.70 (4.04–8.04)	9.06 (5.89–13.92)
25–50th	2.13 (1.58–2.87)	1.80 (1.24–2.61)	3.17 (2.01–5.00)
50–75th	1.44 (1.06–1.96)	1.24 (0.85–1.82)	2.01 (1.23–3.26)
≥ 75th	Reference	Reference	Reference

Number of household members

1	2.25 (1.60–3.18)	1.29 (0.74–2.18)	3.91 (2.36–6.47)
2	2.40 (1.79–3.22)	2.34 (1.62–3.40)	2.50 (1.56–3.99)
3	0.93 (0.67–1.30)	0.91 (0.60–1.38)	0.92 (0.55–1.54)
4	0.56 (0.39–0.80)	0.56 (0.36–0.89)	0.50 (0.27–0.91)
≥ 5	Reference	Reference	Reference
Residence area			
Urban	Reference	Reference	Reference
Rural	1.53 (1.25–1.87)	1.39 (1.07–1.81)	1.74 (1.33–2.29)
Smoking status			
Self-reported			
Non-smoker	Reference	Reference	Reference
Ex-smoker	2.69 (2.24–3.24)	3.30 (2.43–4.49)	2.00 (1.26–3.16)
Smoker	0.99 (0.79–1.24)	1.23 (0.87–1.72)	0.61 (0.35–1.08)
Cotinine-verified			
Non–smoker	Reference	Reference	Reference
Smoker	0.67 (0.55–0.83)	0.56 (0.43–0.71)	0.50 (0.32–0.79)
Survey-cotinine verified			
Non-smoker	Reference	Reference	Reference
Ex-smoker	2.79 (2.30–3.38)	3.37 (2.46–4.60)	2.25 (1.39–3.63)
Smoker	0.92 (0.74–1.15)	1.19 (0.85–1.67)	0.53 (0.34–0.84)
Body mass index			
< 23	Reference	Reference	Reference
23–25	1.49 (1.19–1.87)	1.13 (0.84–1.51)	1.98 (1.42–2.77)
≥ 25	1.88 (1.55–2.29)	1.35 (1.03–1.77)	2.70 (2.02–3.59)
Hypertension			
No	Reference	Reference	Reference
Yes	5.60 (4.71–6.67)	4.24 (3.34–5.38)	8.18 (6.24–10.74)
Diabetes			
No	Reference	Reference	Reference
Yes	5.36 (4.47–6.42)	5.89 (4.62–7.50)	4.41 (3.36–5.78)

Table 5. Adjusted odds ratios and 95% confidence intervals for myocardial infarction and stroke prevalence.

Characteristics	Self–reported	Cotinine–verified	Survey–cotinine verified
Sex			
Male	1.70 (1.26–2.27)	2.39 (1.93–2.94)	1.78 (1.35–2.35)
Female	Reference	Reference	Reference
Age			
< 50	Reference	Reference	Reference
50–59	4.88 (3.12–7.65)	4.89 (3.11–7.69	4.84 (3.09–7.59)
60–69	8.52 (5.41–13.44)	8.52 (5.38–13.48)	8.42 (5.33–13.30)
≥ 70	9.81 (6.05–15.92)	9.78 (6.01–15.92)	9.64 (5.93–15.67)
Marital status			
Married	Reference	Reference	Reference
Single (separated or divorced)	0.97 (0.73–1.28)	0.99 (0.75–1.30)	0.97 (0.74–1.28)
Never-married	0.75 (0.36–1.54)	0.69 (0.34–1.43)	0.74 (0.36–1.52)
Employment status			
Employed	Reference	Reference	Reference
Unemployed	1.90 (1.55–2.33)	1.93 (0.57–2.38)	1.90 (1.55–2.34)
Education			
< High school	1.78 (1.29–2.45)	1.80 (1.30–2.48)	1.79 (1.30–2.47)
High school	1.36 (0.96–1.93)	1.38 (0.98–1.94)	1.37 (0.97–1.93)
> High school	Reference	Reference	Reference
Monthly family income			
< 25th	1.69 (1.24–2.30)	1.70 (1.25–2.32)	1.70 (1.25–2.32)
25–50th	1.25 (0.91–1.72)	1.25 (0.91–1.72)	1.25 (0.91–1.72)
50–75th	1.27 (0.92–1.76)	1.28 (0.93–1.77)	1.27 (0.92–1.76)
≥ 75th	Reference	Reference	Reference
Number of household members			
1	0.94 (0.65–1.37)	0.95 (0.65–1.38)	0.94 (0.65–1.38)
2	0.95 (0.68–1.32)	0.96 (0.69–1.34)	0.95 (0.68–1.33)
3	0.82 (0.58–1.17)	0.82 (0.58–1.18)	0.82 (0.58–1.18)
4	0.82 (0.56–1.20)	0.82 (0.56–1.20)	0.82 (0.56–1.21)
≥ 5	Reference	Reference	Reference
Residence area			
Urban	Reference	Reference	Reference
Rural	1.13 (0.91–1.40)	1.12 (0.90–1.39)	1.13 (0.91–1.40)
Smoking status			

	Self–reported	Cotinine–verified	Survey–cotinine verified
Self-reported			
Non-smoker	Reference	–	–
Ex-smoker	1.62 (1.20–2.19)	–	–
Smoker	1.25 (0.92–1.70)	–	–
Cotinine-verified			
Non-smoker	–	Reference	–
Smoker	–	0.88 (0.69–1.11)	–
Survey-cotinine verified			
Non-smoker	–	–	Reference
Ex-smoker	–	–	1.57 (1.16–2.12)
Smoker	–	–	1.15 (0.87–1.53)
Body mass index			
< 23	Reference	Reference	Reference
23–25	1.10 (1.20–2.19)	1.10 (0.87–1.40)	1.10 (0.86–1.40)
≥ 25	1.25 (0.92–1.70)	1.24 (0.99–1.56)	1.24 (0.99–1.56)
Hypertension			
No	Reference	Reference	Reference
Yes	2.06 (1.69–2.50)	2.05 (1.69–2.50)	2.05 (1.69–2.49)
Diabetes			
No	Reference	Reference	Reference
Yes	1.85 (1.52–2.25)	1.86 (1.53–2.27)	1.85 (1.52–2.26)

*Adjusted for sex, age, marital status, employment status, education level, monthly family income, number of household members, residence area, smoking status, body mass index, hypertension and diabetes.

Table 6. Adjusted odds ratios and 95% confidence intervals for myocardial infarction and stroke prevalence in male participants.

Characteristics	Self–reported	Cotinine–verified	Survey–cotinine verified
Age			
< 50	Reference	Reference	Reference
50–59	4.63 (2.66–8.06)	4.70 (2.70–8.20)	4.60 (2.64–8.01)
60–69	8.65 (4.93–15.18)	8.80 (5.01–15.45)	8.57 (4.87–15.07)
≥ 70	8.09 (4.33–15.10)	8.17 (4.37–15.27)	7.97 (4.25–14.94)
Marital status			
Married	Reference	Reference	Reference
Single (separated or divorced)	1.01 (0.62–1.65)	1.02 (0.63–1.67)	1.01 (0.62–1.65)

Never-married	0.72 (0.30–1.74)	0.67 (0.28–1.61)	0.72 (0.30–1.72)
Employment status			
Employed	Reference	Reference	Reference
Unemployed	1.92 (1.44–2.56)	1.96 (1.47–2.61)	1.93 (1.45–2.57)
Education			
< High school	1.74 (1.20–2.52)	1.76 (1.22–2.55)	1.75 (1.21–2.53)
High school	1.39 (0.93–2.07)	1.40 (0.94–2.09)	1.39 (0.93–2.08)
> High school	Reference	Reference	Reference
Monthly family income			
< 25th	1.71 (1.14–2.57)	1.71 (1.14–2.57)	1.72 (1.15–2.58)
25–50th	1.11 (0.75–1.65)	1.11 (0.74–1.65)	1.11 (0.75–1.66)
50–75th	1.15 (0.77–1.72)	1.15 (0.77–1.73)	1.15 (0.76–1.72)
≥ 75th	Reference	Reference	Reference
Number of household members			
1	0.77 (0.41–1.45)	0.78 (0.41–1.46)	0.77 (0.41–1.45)
2	0.90 (0.59–1.38)	0.92 (0.60–1.40)	0.91 (0.59–1.39)
3	0.78 (0.50–1.22)	0.78 (0.50–1.23)	0.78 (0.50–1.23)
4	0.84 (0.52–1.36)	0.85 (0.52–1.37)	0.85 (0.52–1.37)
≥ 5	Reference	Reference	Reference
Residence area			
Urban	Reference	Reference	Reference
Rural	1.07 (0.80–1.42)	1.06 (0.80–1.41)	1.07 (0.80–1.42)
Smoking status			
Self-reported			
Non-smoker	Reference	–	–
Ex-smoker	1.45 (1.04–2.04)	–	–
Smoker	1.17 (0.81–1.67)	–	–
Cotinine-verified			
Non-smoker	–	Reference	–
Smoker	–	0.87 (0.65–1.15)	–
Survey-cotinine verified			
Non-smoker	–	–	Reference
Ex-smoker	–	–	1.43 (1.02–2.02)
Smoker	–	–	1.12 (0.78–1.60)
Body mass index			
< 23	Reference	Reference	Reference
23–25	1.11 (0.80–1.53)	1.11 (0.80–1.54)	1.10 (0.80–1.53)
≥ 25	1.37 (0.99–1.89)	1.37 (0.99–1.89)	1.36 (0.98–1.89)
Hypertension			
No	Reference	Reference	Reference

Yes	1.84 (1.41–2.40)	1.85 (1.41–2.41)	1.84 (1.41–2.39)
Diabetes			
No	Reference	Reference	Reference
Yes	2.26 (1.72–2.97)	2.29 (1.74–3.01)	2.26 (1.72–2.98)

*Adjusted for age, marital status, employment status, education level, monthly family income, number of household members, residence area, smoking status, body mass index, hypertension and diabetes.

Table 7. Adjusted odds ratios and 95% confidence intervals for myocardial infarction and stroke prevalence in female participants.

Characteristics	Self-reported	Cotinine-verified	Survey-cotinine verified
Age			
< 50	Reference	Reference	Reference
50–59	5.46 (2.32–12.87)	4.98 (2.11–11.77)	5.35 (2.27–12.57)
60–69	8.80 (3.58–21.64)	7.87 (3.18–19.49)	8.56 (3.49–20.99)
≥ 70	13.25 (5.28–33.30)	11.91 (4.71–30.12)	12.83 (5.13–32.11)
Marital status			
Married	Reference	Reference	Reference
Single (separated or divorced)	0.86 (0.60–1.23)	0.91 (0.65–1.29)	0.87 (0.61–1.24)
Never-married	0.74 (0.17–3.25)	0.75 (0.16–3.45)	0.74 (0.17–3.20)
Employment status			
Employed	Reference	Reference	Reference
Unemployed	2.00 (1.46–2.74)	2.04 (1.49–2.80)	2.01 (1.47–2.76)
Education			
< High school	2.06 (0.99–4.29)	2.09 (1.01–4.35)	2.08 (1.01–4.33)
High school	143 (0.71–2.88)	1.44 (0.72–2.90)	1.45 (0.72–2.92)
> High school	Reference	Reference	Reference
Monthly family income			
< 25th	1.79 (1.09–2.91)	1.84 (1.13–3.00)	1.80 (1.10–2.94)
25–50th	1.62 (0.98–2.67)	1.61 (0.98–2.66)	1.63 (0.99–2.68)
50–75th	1.59 (0.95–2.67)	1.61 (0.96–2.69)	1.60 (0.95–2.67)
≥ 75th	Reference	Reference	Reference
Number of household members			
1	1.12 (0.63–1.98)	1.11 (0.63–1.94)	1.12 (0.63–1.98)
2	1.06 (0.61–1.85)	1.06 (0.61–1.84)	1.07 (0.61–1.86)

3	0.91 (0.51–1.64)	0.90 (0.50–1.61)	0.92 (0.51–1.65)
4	0.77 (0.40–1.49)	0.76 (0.40–1.46)	0.78 (0.40–1.49)
≥ 5	Reference	Reference	Reference
Residence area			
Urban	Reference	Reference	Reference
Rural	1.21 (0.90–1.63)	1.19 (0.88–1.59)	1.21 (0.90–1.63)
Smoking status			
Self-reported			
Non-smoker	Reference	–	–
Ex-smoker	2.74 (1.59–4.71)	–	–
Smoker	0.96 (0.53–1.72)	–	–
Cotinine-verified			
Non-smoker	–	Reference	–
Smoker	–	1.19 (0.88–1.59)	–
Survey-cotinine verified			
Non-smoker	–	–	Reference
Ex-smoker	–	–	2.92 (1.64–5.18)
Smoker	–	–	0.90 (0.56–1.44)
Body mass index			
< 23	Reference	Reference	Reference
23–25	1.09 (0.77–1.56)	1.08 (0.76–1.54)	1.08 (0.76–1.54)
≥ 25	1.05 (0.77–1.44)	1.06 (0.78–1.44)	1.05 (0.77–1.43)
Hypertension			
No	Reference	Reference	Reference
Yes	2.43 (1.80–3.28)	2.41 (1.78–3.25)	2.43 (1.80–3.28)
Diabetes			
No	Reference	Reference	Reference
Yes	1.29 (0.97–1.74)	1.31 (0.98–1.75)	1.29 (0.96–1.73)

*Adjusted for age, marital status, employment status, education level, monthly family income, number of household members, residence area, smoking status, body mass index, hypertension and diabetes.