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Association of heating fuel types with mortality and cardiovascular events among non-smokers in China $a{a}$

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ABSTRACT

Only a few prospective studies have investigated the relationship between solid fuel use and cardiovascular disease (CVD) and mortality, and they have reported inconsistent conclusions. This study aimed to investigate the effect of solid fuel heating on the risk of CVD events and all-cause mortality among non-smokers. Data of this sub-study were obtained from the China Hypertension Survey (CHS), and 13,528 non-smoking participants aged 35 or above without self-reported medical history of CVD were enrolled between October 2012 and December 2015. CVD events and all-cause mortality were followed up in 2018 and 2019. The type of primary heating fuel was categorized as clean fuel (natural gas and electricity) and solid fuel (coal, wood, and straw). Cox regression was applied to evaluate the relationship between solid fuel use and CVD events and all-cause mortality. Of the 13,528 non-smoking participants, the mean age was 55.4 \pm 13.1 years. During the median follow-up of 4.93 years, 424 participants developed fatal or nonfatal CVD (stroke, 273; coronary heart disease, 119; and other cardiovascular events, 32) and 288 died from all causes. The cumulative incidence of fatal and nonfatal CVD and all-cause mortality were 6.78 and 4.62 per 1000 person-years, respectively. Solid fuel heating was independently associated with an increased risk of fatal or nonfatal stroke and all-cause mortality compared with the use of clean fuels, the fully adjusted hazard ratios (HRs), and 95% confidence intervals (CI) were 1.44 (1.00-2.08) and 1.55 (1.10-2.17), respectively. The relationship between solid fuel heating and fatal and nonfatal CVD events was non-significant (HR = 1.19; 95% CI: 0.89-1.59). Solid fuel heating is longitudinally associated with a higher risk of stroke and all-cause mortality in non-smoking Chinese. Switching to cleaner energy sources for heating may be important for reducing the risk of CVD and mortality.

1. Introduction

The World Health Organization (WHO) has estimated that approximately 3 billion people worldwide rely on highly polluting fuels, including coal, wood, and crop waste, which are often burned inefficiently in poorly ventilated cooking environments, emitting large amounts of air pollutants such as carbon monoxide, nitrogen dioxide and particulate matter within households (Global Health Observatory, 2018; Amegah and Jaakkola, 2016). Emissions from burning solid fuels for cooking and heating are a major contributor to the global burden of disease, with household air pollution responsible for 1.8 million deaths and 60.9 million disability-adjusted life-years (DALYs) in 2017 world-wide, particularly in low- and middle-income countries, including China (Lee et al., 2020; Murray et al., 2020). Cardiovascular disease (CVD) is

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the leading cause of death worldwide, and accounts for 0.3 million death and 9.5 million DALYs caused by household air pollution (Lee et al., 2020).

Despite the large population using solid fuels and the severe disease burden of household air pollution, only a few prospective studies have investigated the relationship between solid fuel use and CVD and mortality and have reported inconsistent results. Previous study in the Chinese population have shown that solid fuel use was associated with a higher risk of CVD death and all-cause mortality, whereas inconsistent conclusions were obtained regarding stroke mortality (Yu et al., 2020; Yu et al., 2018; Kim et al., 2016). However, the Golestan Cohort Study in northeastern Iran found no association between use of wood for cooking and 10-year CVD mortality and all-cause mortality (Mitter et al., 2016). Moreover, the PURE study also failed to find an association of solid fuel use with CVD mortality and all-cause mortality among never smokers (Hystad et al., 2019). Moreover, most existing studies only focused on mortality as an end points, and evidence for the effect of solid fuel use on fatal and nonfatal cardiovascular events is scarce. To our knowledge, only one prospective cohort study examined the associations between solid fuel use and fatal or non-fatal CVD events and found non-significant association (Hystad et al., 2019). In addition, given the differences in exposure patterns and the residual confounding caused by smoking, few studies have specifically focused on the association between solid fuel for heating and CVD and all-cause mortality in non-smokers. Therefore, it is necessary to conduct a prospective study to better clarify the association between solid fuel for heating and the risk of fatal and non-fatal CVD events and all-cause mortality among non-smokers in China.

2. Materials and methods

2.1. Study design and population

Data of this investigation were obtained from the China Hypertension Survey (CHS), which was described previously (Wang et al., 2018a; Wang et al., 2014; Hao et al., 2019). Briefly, the CHS study was conducted from October 2012 to December 2015, in a nationally representative sample of 0.5 million participants aged 15 years or older that was obtained by using a stratified, multistage random sampling method in 31 provinces in mainland China. For this sub-study, we further stratified the selected urban and rural areas into eastern, central, and western regions according to their geographical location and economic level, and 16 cities and 17 counties were selected using a simple random sampling method (Wang et al., 2018b). Three or more communities or villages were then selected from each region, and 35,000 subjects aged ≥35 years were randomly selected. Finally, 30,036 individuals who completed the health examinations from 2012 to 2015 in the baseline survey were followed up in 2018-2019 (median follow-up, 4.93 years). After excluding 9232 ever-smokers (including current-smokers and ex-smokers), 3518 participants who dropped out during the follow-up and 1318 participants with medical history of CVD (coronary heart disease, stroke and other heart diseases that are not clearly defined) at baseline. Then we excluded 2440 participants with missing data on primary heating fuel. Finally, a total of 13,528 participants were included in the present analysis. Each participant provided written informed consent and this study was approved by the Ethics Committee of Fuwai Hospital (Beijing, China).

2.2. Measurement and data collection

A standardized questionnaire was used to collect information on demographic characteristics, lifestyle risk factors, and medical history by well-trained interviewers. Height and weight were measured using a standardized right-angle device and an OMRON body fat and weight measurement device (V-body HBF-371, Omron, Japan) with participants wearing thin clothing and no shoes. Body Mass Index (BMI) was calculated by dividing weight (kg) by height squared (m²). Blood pressure of the participant was measured using the Omron HBP-1300 professional portable blood pressure monitor (Omron, Kyoto, Japan) on the right arm in the sitting position after resting for at least 5 min. Laboratory examinations were performed on venous blood samples collected after at least 8 h of overnight fasting. Fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) levels were measured by a central core laboratory (Beijing Adicon Clinical Laboratories, Inc., Beijing, China).

2.3. Assessments of solid fuel exposure and covariates

Primary heating fuel was categorized as clean fuel (natural gas and electricity) and solid fuel (coal, wood, charcoal and straw). Information on indoor ventilation was collected through self-reporting and the classification of ventilation frequencies included never, <5 days/week, \geq 5 days/week according to the answers of the participants.

We classified the age of participants into five groups: 35–44, 45–54, 55–64, 65–74, and >75 years old. BMI was divided into $<18.50 \text{ kg/m}^2$, 18.50–23.9 kg/m², 24.00–27.9 kg/m², and >28 kg/m², representing underweight, normal weight, overweight and obese, respectively (Chen and Lu, 2004). Educational levels were categorized into two groups: middle-high school or lower and high school or above. Employment status was classified as employed, retired, students and unemployed. Family history of CVD was defined as having at least one parent or siblings with a medical history of coronary heart disease or stroke. Diabetes was defined as a self-reported medical history of T2DM and/or an FPG level >7.0 mmol/L (126 mg/dL) and/or taking anti-diabetic medications (American Diabetes Associa, 2020; Chinese Diabetes Society., 2018). Participants with TC \geq 6.2 mmol/L, TG \geq 2.3 mmol/L, LDL-C > 4.1 mmol/L, or HDL-C < 1.0 mmol/L were considered as having dislipidemia (Zhu et al., 2016). We also collected some socio-economic status (SES) indicators at district/county levels, including average education years and per capita Gross Domestic Product (GDP), from statistic yearbooks, demographic census of China at 2000, national bureau of statistics and China national knowledge infrastructure. Kitchen ventilation and solid fuels for cooking were also obtained. Moreover, we obtained the average fine particulate matter (PM2.5, particles with an aerodynamic diameter of \leq 2.5 µm) concentrations annually from an air quality reanalysis dataset for China covering 2013 to 2018, which has spatial (15 km) and temporal (1 h) resolutions and was produced by the chemical data assimilation system (ChemDAS) developed by the Institute of Atmospheric Physics, Chinese Academy of Sciences. The qualities of this dataset have been cross-validated, indicating a high accuracy. The bilinear interpolation was conducted to obtain the address-based exposure of individuals according to his/her residential county/district and the survey year (Kong et al., 2021).

2.4. Follow-up and outcome measures

Fatal and nonfatal CVD events and mortality were followed up in 2018 and 2019 via interviewing participants or their proxies in-person, or via telephone or mail questionnaires, and we further checked medical records for reconfirmation. Local investigators initially recorded the cardiovascular events and deaths of the participants, and then hospital records and death certification were reviewed by the central adjudication committee of Fuwai Hospital (Beijing, China) to determine the final diagnosis. Cardiovascular events were defined as coronary heart disease (CHD, ICD-10 code I20–I25), stroke (I60–I61 and I63–I64), chronic heart failure (I50), and death due to CVD (I00–I25, I27–I88, and I95-99). Stroke included non-fatal stroke and fatal stroke (subarachnoid hemorrhage, intracerebral hemorrhage, ischemic stroke, unspecified stroke). CHD was defined as non-fatal CHD (including myocardial infarction, coronary artery bypass graft surgery, or percutaneous coronary

intervention) and fatal CHD (such as fatal myocardial infarction and other coronary deaths). Mortality outcomes included all-cause mortality and cause-specific mortality (Died of CVD, stroke, or CHD, respectively). Causes of death were classified by trained healthcare staff according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10).

2.5. Statistical analysis

Continuous variables were described as means \pm standard deviation (SD) and categorical variables as frequency and percentages by category of heating exposure. The *t*-test and χ^2 test were used to compare continuous and categorical variables between the different groups, respectively. Multivariable Cox model was used to quantify the association between solid fuel use and the risk of CVD and all-cause mortality. The Cox proportional hazard assumption were tested by weighted Schoenfeld residuals and P-values were greater than 0.05 for all outcomes. For all analyses, we built three steps forward multivariableadjusted models to assess the relationship between solid fuel use and the CVD risk and all-cause mortality. In model 1, we adjusted for age, sex, BMI, alcohol consumption, educational level, employment status (employed, retired, students, or unemployed), urbanization (urban and rural), geographical region (east, central and western); Model 2 included all Model 1 covariates plus hypertension, diabetes, hypercholesterolemia, and family history of CVD; in Model 3, we further adjusted for second-hand smoke (yes or no), the annual average outdoor PM2.5 concentrations (continuous) at baseline, solid fuels use for cooking, kitchen ventilation, indoor ventilation (yes or no), average years of education and per capita Gross Domestic Product (GDP) at district/ county levels. Moreover, we conducted stratified analyses by age (>60, <60 years old), sex, urbanization, outdoor PM2.5 concentrations (<50, \geq 50 µg/m³), and BMI (<24, \geq 24 kg/m²) using Model 3.

Several sensitivity analyses were implemented to assess the robustness of our findings based on our fully adjusted model (Model 3). First, we used competing-risks regression based on Fine and Gray's proportional sub-hazards model to evaluate the association of heating fuel type with the risk of CVD events given that the potential impact of noncardiovascular death as competing risk events rather than censoring (Austin et al., 2016; Wolbers et al., 2014). The sub-distribution hazard ratio (SHR) was computed from the Fine-Gray model (Abbas et al., 1999). Second, we removed covariates that might be on the causal pathway to household air pollution (HAP) and outcome events, including hypertension, dyslipidemia, and diabetes. Additionally, we removed outdoor PM2.5 concentrations because emissions from the burning of solid fuels also affect the levels of ambient air pollution (Chafe et al., 2014). Other sensitivity analyses were implemented by excluding subjects aged 80 years old or above at baseline and participants with co-morbidities at baseline, respectively. We defined co-morbidity as any combination of two or more of three diseases: diabetes, hypertension and hypercholesterolemia following previous study (Zhang et al., 2019).

The missing values on age, gender, residence, body mass index (BMI), indoor ventilation, lifestyle factors and history of diseases were handled using multiple imputations (MI). The comparison of data set before and after the MI was demonstrated in Table A1. Analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC, USA), and a 2-tailed level of 0.05 was statistically significant.

3. Results

3.1. Characteristics of the study

Of the 13,528 non-smoking participants, the mean (SD) and median (Interquartile range, IQR) age were 55.4 \pm 13.1 and 54 \pm 22 years, respectively. Fig. 1 showed the flow chart of this study. During the follow-up period, 424 participants developed fatal or nonfatal CVD

Table 1

Characteristics of study participants by heating fuels types.

Characteristic	All participants	Clean fuels (N	Solid fuels (N	P value
	(13328)	= 9139)	= 4309)	
Age, years	55.4 ± 13.1	55.5 ± 13.4	55.3 ± 12.4	0.436
Gender, %				0.046
Male	3522 (26.0)	2337	1185	
		(25.5)	(27.1)	
Female	10006 (74.0)	6822	3184	
		(74.5)	(72.9)	
Educational level, %				<.001
Elementary middle	7191 (53.2)	4255	2936	
School or lower		(46.5)	(67.2)	
High school or above	6337 (46.8)	4904	1433	
		(53.5)	(32.8)	
Residence, %	(100 (45 5)		1000	<.001
Urban	6189 (45.7)	5151	1038	
Burgel	7220 (54.2)	(50.2)	(23.8)	
Kurai	/339 (34.3)	4008	3331	
Pagion %		(43.8)	(70.2)	< 001
Foot	EE02 (40 7)	4074	E-29	<.001
East	5502 (40.7)	(54.2)	(12.1)	
Control	EE02 (41.2)	2405	(12.1)	
Cellual	5595 (41.5)	(37.2)	(50.1)	
West	2422 (18.0)	(37.2)	1652	
west	2433 (18.0)	780 (8.3)	(37.8)	
Consumption of Alcohol	1836 (13.6)	1432	(37.8)	< 001
%	1000 (10.0)	(15.6)	404 (9.2)	<.001
Hypertension %	5149 (38.1)	3465	1684	0.418
hypertension, //	5115 (50.1)	(37.8)	(38.5)	0.110
Hypercholesterolemia, %	4537 (33.5)	3084	1453	0.727
	,	(33.7)	(33.3)	
Diabetes, %	1330 (9.8)	987	343 (7.9)	<.001
,		(10.8)		
Ventilation, %				<.001
Never	228 (1.7)	110 (1.2)	118 (2.7)	
<5 days/week	1716 (12.7)	606 (6.6)	1110	
-			(25.4)	
≥5 days/week	11584 (85.6)	8443	3141	
		(92.2)	(71.9)	
Kitchen ventilation, %	11865 (87.7)	8254	3611	<.001
		(90.1)	(82.7)	
PM2.5, μg/m ³	61.5 ± 23.5	63.7 \pm	56.8 \pm	<.001
		20.0	28.9	
BMI, Kg/m ²	24.71 ± 3.53	$24.76~\pm$	$24.61~\pm$	0.022
		3.48	3.53	
Family history of CVD, %	1972 (14.6)	1558	414 (9.5)	<.001
		(17.0)		

BMI, body mass index; PM2.5, particles with an aerodynamic diameter of \leq 2.5 μ m; CVD, cardiovascular disease.

(stroke, 273; CHD, 119; and other cardiovascular events, 32) and 288 died from all causes. The cumulative incidence of fatal and nonfatal CVD and all-cause mortality were 6.78 and 4.62 per 1000 person-years, respectively. The characteristics of participants at baseline according to heating fuel types have been summarized in Table 1. Overall, about 32% of the participants report using solid fuels for heating. In general, solid fuel heating users were less educated and more likely to live in rural and central and western areas compared with clean fuel users. The duration and frequency of indoor ventilation were slightly lower among solid fuel users for heating. Individuals who reported using solid fuels were noted to lower BMI and the prevalence of diabetes among solid fuel users and clean fuel users was 7.9% and 10.8%, respectively.

3.2. Association between solid fuels heating and CVD events

Table 2 presents the relationship between solid fuel use and the risk of CVD events. In the multivariable-adjusted models, the association between solid fuel use and fatal and nonfatal CVD was relatively weak in Model 1, and adjusted HRs (95%CI) for fatal and non-fatal CVD and



Fig. 1. Flowchart of inclusion and exclusion of study participants and the incidence of CVD events and mortality during follow-up. CVD, cardiovascular disease; CHD, coronary heart disease.

stroke were 1.22 (95% CI: 0.94–1.58) and 1.46 (95% CI: 1.05–2.01), respectively. The similar results were obtained in Model 2. Although the association between solid fuel heating and fatal and nonfatal CVD was not statistically significant in Model 3 (HR (95%CI): 1.19 (0.89–1.59)), solid fuel users had an increased risk of stroke compared to those who used clean fuel heating (HR = 1.44; 95%CI:1.00–2.08).

3.3. Association between solid fuel heating and mortality

The risk of CVD mortality was associated with solid fuels use in Model 1 and Model 2, with the adjusted HRs (95%CI) of 1.67 (1.08–2.60) and 1.66 (1.08–2.58), respectively (Table 2). However, the adjusted HR (95%CI) was 1.31 (0.81–2.13) when PM2.5, solid fuel for cooking, indoor ventilation, average years of education and GDP were adjusted in the Model 3. The risk of fatal stroke for solid fuel users was significantly increased, however, the statistical power may be limited due to the relatively small number of outcome events. For all-cause mortality, the associations were statistically significant in Model 1 and Model 2, the HRs (95%CI) were 1.84 (1.37–2.48) and 1.86 (1.38–2.50), respectively. The association between solid fuel heating and all-cause mortality among non-smokers was weakened when we further adjusted for other possible sources of indoor and outdoor pollution in Model 3 (HR (95%CI): 1.55 (1.10–2.17)).

3.4. Stratified analysis and effect modification

Stratified analyses were illustrated in Fig. 2. The associations of solid fuel use with CVD events and all-cause mortality did not change substantially across most subgroups. However, we observed a slightly different association between solid fuel heating and CVD events in the rural areas (HR = 1.61; 95%CI:1.04,2.48) and in urban area (HR = 0.69; 95%CI:0.42,1.14), and the *P* interaction was 0.070. Similar results were observed for all-cause mortality. In addition, for CVD events and all-cause mortality, subjects living in different concentrations of PM2.5 had a greater significant effect modification of solid fuel use, and the *P* values of multiplicative interactions were 0.006 and 0.002, respectively.

3.5. Sensitivity analyses

Table 3 shows the results of the sensitivity analyses. For CVD risk, the conclusions were consistent after non-cardiovascular death was considered as a competing risk event rather than the censored based on the Fine-Gray model, the HRs were 1.21 (0.91–1.59) for all CVD, 1.47 (1.04–2.07) for stroke, and 0.61 (0.35–1.06) for CHD. When we removed baseline chronic conditions including hypertension, diabetes, and dyslipidemia, or removed outdoor PM2.5 from Model 3 alone, the effect estimates of solid fuel heating on CVD events did not change substantially. However, when individuals older than 80 years or with comorbidity at baseline were excluded, the risk of all-cause mortality was slightly increased.

4. Discussions

This nationally prospective study demonstrated that solid fuel use for heating was independently associated with an increased risk of fatal or nonfatal stroke and all-cause mortality among non-smokers in China compared with the use of clean fuels, whereas a non-significant relationship was found between solid fuel heating and fatal or nonfatal CVD events.

This current study contributes to the evidence of an association between solid fuel use and the risk of CVD events and all-cause mortality in a non-smoking population. Up to now, only a few prospective studies have examined the relationship between solid fuel use and CVD and mortality, particularly when solid fuel use is examined separately for cooking and heating. The China Kadoorie Biobank study enrolling 271,217 participants with a 7.5 year of follow-up showed that use of solid fuels for heating was associated with increased risk of CVD mortality (HR, 1.63 [95%CI: 1.51,1.75]) and all-cause mortality (HR, 1.35 [95%CI: 1.28,1.43]) among never-smokers compared with clean fuel use (Yu et al., 2018). Another longitudinal study recruiting participants from the Shanghai Women's Health Study cohort reported that the estimated HR for participants who use coal for cooking compared to

Table	2
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Association of solid fuel for heating with cardiovascular disease and mortality among nonsmokers.

	Events	Incidence/1000	Model 1	Model 2	Model 3
		person-years	HR (95% CI)	HR (95% CI)	HR (95% CI)
CVD (fatal + nonfatal)	424	6.78	1.22 (0.94–1.58)	1.23 (0.95–1.58)	1.19 (0.89–1.59)
Stroke	273	4.33	1.46 (1.05-2.01)	1.45 (1.05-2.00)	1.44 (1.00-2.08)
CHD	119	1.88	0.69 (0.41-1.14)	0.69 (0.42-1.16)	0.60 (0.36–1.04)
Cause-specific mortality					
CVD	132	2.09	1.67 (1.08-2.60)	1.66 (1.08-2.58)	1.31 (0.81-2.13)
Stroke	53	0.84	2.36 (1.19-4.66)	2.31 (1.17-4.54)	2.26 (0.98-5.21)
CHD	50	0.79	0.92 (0.43-1.95)	0.92 (0.43-1.96)	0.59 (0.28-1.27)
All-cause mortality	288	4.62	1.84 (1.37-2.48)	1.86 (1.38-2.50)	1.55 (1.10-2.17)

HR, hazard ratio; CVD, cardiovascular disease; CHD, coronary heart disease.

Model 1: adjusted for age, sex, BMI, alcohol consumption, educational level, employment status, urbanization and geographical region.

Model 2: model 1 plus hypertension, diabetes, hypercholesterolemia and family history of CVD.

Model 3: model 2 plus secondhand smoke, the annual average outdoor PM2.5 concentrations (continuous) at baseline, solid fuel use for cooking, kitchen and indoor ventilation, and average years of education and per capita Gross Domestic Product (GDP) at district/county levels.

Subgroup	Events	HR (95% CI)		P value
Fatal and non-fatal CVD				
Age, vears				0.116
< 60	93	1.27 (0.73-2.18)	⊧ ∔∎ i	
≥ 60	331	1.12 (0.80-1.58)	⊢∎⊸i	
Gender		, , ,		0.414
Male	145	1.14 (0.67-1.94)	⊢ ∎ —-1	
Female	279	1.20 (0.85-1.70)	⊢∎⊸i	
Residence		. ,		0.070
Urban	213	0.69 (0.42-1.14)	⊢∎ -+	
Rural	211	1.61 (1.04-2.48)	⊢ ∎i	
Outdoor PM2.5, µg/m ³				0.006
< 50	121	0.50 (0.19-1.31)	⊢∎──┤	
≥ 50	303	1.02 (0.74-1.42)	⊢∎⊣	
BMI, Kg/m ²				
< 24	121	2.11 (1.20-3.71)	⊢−− ■−−−−−1	0.069
≥ 24	303	0.96 (0.68-1.36)	H - -1	
All-cause mortality				
Age, years				0.101
< 60	38	1.07 (0.42-2.73)	⊢ ∎ i	
≥ 60	250	1.56 (1.08-2.26)	⊢ ∎i	
Gender		. ,		0.410
Male	104	1.61 (0.88-2.94)	⊢ ∎−−−1	
Female	184	1.51 (1.00-2.29)		
Residence		, ,		0.016
Urban	96	0.52 (0.27-0.98)	⊢∎⊸∢	
Rural	192	3.86 (2.10-7.07)		
Outdoor PM2.5, µg/m ³				0.002
< 50	113	1.68 (0.43-6.60)	⊢∎ →	
≥ 50	175	1.31 (0.87-1.97)	⊢ ∎1	
BMI, Kg/m ²		. ,		
< 24	123	1.69 (0.97-3.00)	⊢ ∎−−−1	0.655
≥ 24	165	1.47 (0.95-2.28)		
			0 0.5 1 1.5 2 2.5 3 3.5 4	

Fig. 2. Stratified analyses of association between indoor solid fuel heating and cardiovascular events and all-cause mortality among non-smokers. BMI, body mass index; PM2.5, particles with an aerodynamic diameter of \leq 2.5 µm; CVD, cardiovascular disease.

those who never use coal was 1.12 (95%CI: 1.05,1.21) for all-cause mortality and 1.18 (95%CI: 1.02, 1.37) for CVD mortality, but found no association for stroke mortality with an HR being 1.01 (95%CI: 0.84, 1.22) (Kim et al., 2016). In northeastern Iran, the Golestan Cohort Study found no association of wood use for cooking with CVD mortality (HR, 1.03 [95%CI: 0.97, 1.08]) and all-cause mortality (HR, 1.01 [95%CI: 0.97, 1.05]). In addition, a multi-national prospective study (PURE) also demonstrated that household air pollution was associated with the increased risk of CVD mortality and all-cause mortality with an HR of 1.09 (95% CI: 1.00, 1.19) and 1.24 (95% CI: 1.14, 1.36), respectively (Yusuf et al., 2020). However, although non-fatal CVD also imposes a large burden on the patient's family and society, most previous studies have focused only on an outcome of fatal CVD, while the evidence for both fatal and non-fatal CVD is relatively scarce. To date, only one epidemiological study based on 11 countries reported the association between solid fuel use and the risk of fatal and non-fatal CVD and all-cause mortality, the estimated HRs were 1.04 (95% CI: 0.91, 1.19) for CVD death, 1.08 (95% CI: 0.99, 1.17) for fatal or nonfatal CVD, 1.12 (95% CI: 0.99, 1.27) for fatal or nonfatal stroke and 1.12 (95% CI: 1.04, 1.21) for all-cause mortality (Hystad et al., 2019). The findings of these studies were consistent for household air pollution and all-cause mortality but differed for CVD deaths. These contradictory results may be

due in part to the different definitions of CVD events and the different time intervals between two adjacent follow-up visits. In comparison, our study was consistent with previous studies for all-cause mortality and found that solid fuel for heating increased the risk of fatal and non-fatal stroke, which enriches the evidence on the health effects of solid fuel use among non-smokers, especially for developing countries.

We observed a modification effect of urbanization and outdoor PM2.5 concentrations on the association between solid fuel for heating and CVD and all-cause mortality. In rural populations, we observed an increased association between solid fuel heating and CVD and all-cause mortality, indicating that those people suffered greater health impairments, which is consistent with previous studies (Yu et al., 2018). Two studies from the China Kadoorie Biobank (CKB) have assessed the solid fuels use and the risk of CVD mortality and all-cause mortality in rural and urban Chinese population, respectively, and the association were both positive (Yu et al., 2020; Yu et al., 2018), which were inconsistent with our findings. Although we adjusted for education level, employment status, average years of education and GDP, there still are some other unmeasured socio-economic indicators correlated with solid fuels use for heating, which could confound the risk estimates of CVD and all-cause mortality (Clark et al., 2009; Stringhini, 2010). Besides, the follow-up time of this current study was relatively short (median:4.94

Table 3

Sensitivity analyzes for the relationship between solid fuels for heating and cardiovascular events and all-cause mortality.

Models ^a	CVD	Stroke	CHD	All-cause mortality			
Competing	Competing risk model						
Clean	Reference	Reference	Reference	-			
fuels							
Solid	1.21	1.47	0.61	-			
fuels	(0.91 - 1.59)	(1.04 - 2.07)	(0.35 - 1.06)				
Removing	Causal Pathway	Variables in Mod	lel 3 ^b				
Clean	Reference	Reference	Reference	Reference			
fuels							
Solid	1.19	1.46	0.60	1.53			
fuels	(0.89 - 1.60)	(1.01 - 2.12)	(0.34 - 1.04)	(1.09 - 2.15)			
Removing outdoor PM2.5 in Model 3							
Clean	Reference	Reference	Reference	Reference			
fuels							
Solid	1.11	1.32	0.63	1.37			
fuels	(0.85–1.46)	(0.93–1.86)	(0.37 - 1.09)	(1.01 - 1.86)			
Excluding participant aged 80 or older							
Clean	Reference	Reference	Reference	Reference			
fuels							
Solid	1.25	1.48	0.68	1.72			
fuels	(0.92–1.69)	(1.00-2.18)	(0.37 - 1.24)	(1.16 - 2.55)			
Excluding participant with co-morbidity at baseline							
Clean	Reference	Reference	Reference	Reference			
fuels							
Solid	1.26	1.65	0.46	1.58			
fuels	(0.88 - 1.80)	(1.05–2.61)	(0.23–0.93)	(1.07 - 2.35)			

CVD, cardiovascular disease; CHD, coronary heart disease.

^a All sensitivity analyses were based on our fully adjusted model (Model 3). ^b Model 3 minus baseline chronic conditions, hypertension, diabetes and dyslipidemia.

years), and thus, we consider further evaluating the association between solid fuels use and health outcomes among urban and rural population, respectively, in a longer follow-up period in the future. Therefore, identifying populations vulnerable to the effects of indoor air pollution is essential for the implementation of prevention strategies and allocation of resources.

Additionally, our study reported that outdoor PM2.5 concentrations could modify the effects of solid fuels on CVD and mortality. One possible reason for this is that indoor air pollution may be easily affected by outdoor air pollution, and indoor solid fuel combustion is also a source of outdoor PM2.5 concentration. As known, solid fuel has been a commonly used as a proxy for household air pollution in previous studies due to the difficulty of real-time monitoring household pollution in large cohort studies (Yu et al., 2018; Mitter et al., 2016; Alam et al., 2012). Importantly, a recent study has shown that the difference of PM2.5 was 110-880 mg/m3 between electricity/gas and biomass kitchens (Shupler et al., 2018), which further supports the use of solid fuels as an indicator of household air pollution in this current study. However, since measurement errors still exist, it is still necessary to supplement regression validation methods to estimate individual exposure more accurately (Weller et al., 2007). Moreover, the type of solid fuels for heating may be affected by seasonality. The percentage of solid fuel for winter heating was higher in rural site than that in urban sites (74%-91% vs 17%), and PM2.5 concentration in cold season was 2.5 times higher than in warm season according to the China Kadoorie Biobank study recruiting three study areas (two rural sites: Henan and Gansu; one urban area: Suzhou) (Chan et al., 2021). In our present study, the PM2.5 concentrations were 55.34 and 24.33 mg/m³ in cold (April to September) and warm season (October to March), respectively. Besides, previous work related with current study demonstrated that long-term temperature variability was associated with the risk of CVD incidence (Kang et al., 2021), and temperature also affects the behavior of winter heating, which may bias the risk estimates of this current study. We consider assessing the effect of seasonality in subsequent studies, using static and wearable devices to evaluate the bias in a small sample size. Possible mechanisms for increased CVD and all-cause mortality risk may include pathways through cardiac autonomic dysfunction and athero-thrombosis (Newby et al., 2015). This may be due to the release of substantial air pollutants such as carbon monoxide, nitrogen dioxide, and PM2.5 by burning solid fuels (Clark et al., 2013; Ni et al., 2016).

There are several major strengths in this study. Firstly, this study was based on a nationally representative survey with standardized procedures and strict quality control. Secondly, our study is the first to assess both fatal and nonfatal CVD associated with solid fuels for heating in a non-smoking population, which mitigates some of the residual confounding factors associated with smoking. Lastly, competitive risk analysis considering death as a competing event was employed to ensure the robust conclusions of association. However, we acknowledge some specific limitations. First, there may be some exposure misclassification in self-reported solid fuel use as a proxy for household air pollution due to the influence of indoor ventilation frequency, climate, and fuel properties (Clark et al., 2013; Gordon et al., 2014) However, we adjusted for indoor ventilation frequency and the outdoor PM2.5 concentration, which may reduce some confounding. Second, information on the duration of solid fuel for heating and solid fuel use during childhood or adolescence were not collected in the current study since they might influence the levels of solid fuel exposure, which could confound the association between solid fuel for heating and CVD events and all-cause mortality risk. Third, although we have adjusted for a wide range of covariates in this study, residual confounding may remain due to the influence of socioeconomic status on the choice of fuel type, which has also been associated with CVD and all-cause mortality (Clark et al., 2009; Wu et al., 2016).

5. Conclusions

In summary, our findings show that the solid fuel for heating use was independently associated with the risk of fatal or nonfatal stroke and allcause mortality in non-smoking Chinese, whereas a non-significant association between solid fuel heating and fatal or nonfatal CVD was observed. This result indicates that switching to cleaner energy sources for heating may be important to further reduce the risk of CVD and allcause mortality.

Author contribution

Cao Xue: Conceptualization, Methodology, Formal analysis, Software, Writing an original draft preparation. Tang Haosu, Zheng Congyi, Kang Yuting and Zhang Linfeng: Data curation, Formal analysis, Software. Wang Xin, Chen Zuo, Zhou Haoqi and Chen Lu: Investigation. Yang Ying and Huang Gang: Software, Validation. Wang Zengwu: Conceptualization, Funding acquisition, Writing-Reviewing and Editing.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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