Cigarette Smoking and All-cause Mortality in Rural Chinese Male Adults: 15-year Follow-up of the Anqing Cohort Study

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Abstract

**Background** — According to the Global Burden of Disease Study 2017, smoking is one of the leading four risk factors contributing to deaths in China. We aimed to evaluate the associations of smoking with all-cause mortality in a Chinese rural population.

**Methods** — Male participants over age 45 (n=5,367) from a large familial aggregation study in rural China, were included in the current analyses. A total of 528 former smokers and 3849 current smokers accounted for 10% and 71.7% of the cohort, respectively. Generalized Estimating Equations were used to evaluate the association between baseline smoking status and mortality, adjusting for pertinent covariates.

**Results** — There were 579 recorded deaths during the 15-year follow-up. Current smokers (odds ratio [OR],1.60; 95% CI,1.23-2.08) had higher all-cause mortality risks than nonsmokers. Relative to nonsmokers, current smokers of more than 40 pack-years ([OR],1.85; 95% CI,1.33-2.56) had a higher all-cause mortality risk. Compared to nonsmokers, current smokers who started smoking before age 20 ([OR],1.91; 95% CI,1.43-2.54) had a higher all-cause mortality risk, and former smokers in the lower pack-year group who quit after age 41 (median) ([OR],3.19; 95% CI,1.83-5.56) also had a higher risk of death after adjustment. Furthermore, former smokers who were also former drinkers had the highest significant risk of mortality than people who never smoke and drink. ($P$ for interaction = 0.034).

**Conclusions** — This study provides evidence that current smokers or former smokers have higher mortality risk than nonsmokers and would benefit from cessation at a younger age.

Introduction

Smoking is a leading, but avoidable, causes of premature deaths and disability globally, contributing to an estimated six million deaths worldwide in 2010, including one million in China. The World Health Organization projects that by 2030 tobacco-attributable deaths will annually account for 3 million deaths in industrialized countries and 7 million in developing countries. China now consumes about 40% of the world’s total cigarettes, predominantly by men, with a large increase in consumption occurring in urban rather than rural areas over the past three decades. During the past 20 years, a slight decrease in smoking prevalence was observed in the general Chinese population the success rate of smoking cessation was only 14.4%, has no significant change compared to 2010. An awareness of the harms of cigarette smoking and the diseases it can cause showed no obvious change from the cessation rates. Despite tobacco control, cigarette use remains the leading cause of premature mortality in China and globally. The 2017 Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) estimated that high systolic blood pressure, smoking and a diet high in sodium were the top three risk factors for number of deaths in 2017 in China. They were also the leading risk factors for disability-adjusted life-years (DALYs) in China overall and in 21 provinces, and were either second or third in all remaining provinces.

The hazards of smoking have been documented over the past 55 years, providing sufficient evidence of a causal relationship between smoking and many types of death. A total of 160,113 participants of the NIH-AARP Diet and Health Study aged >70 years showed that relative to never smokers, current smokers were more...
likely to die during follow-up (hazard ratio, 3.18; 95% CI, 3.04-3.31) \(^8\). For participants who were 25 to 79 years of age in the U.S. National Health Interview Survey, the rate of death from any cause among current smokers was about three times that of those who had never smoked (hazard ratio for men, 2.8; 99% CI, 2.4-3.1) \(^9\). Early initiation of smoking is also related to increased mortality from all causes and disease-specific causes, such as vascular diseases (cardiovascular, coronary artery disease, cerebrovascular disease); respiratory diseases; and cancers \(^10\). In addition, the mortality risk associated with smoking cessation is decreased compared with continuing smokers after 12 years of follow-up in the Nurses’ Health Study. \(^7\)

The China Health and Nutrition Survey (CHNS) study indicated that the current smoking rate in rural villages has remained relatively stable across the past two decades from 2000 (about 50-55%). The rate in urban neighborhoods decreased from 1991 to 2009, and then slightly increased to 25% in 2011 \(^11\). Residents living in socially and economically developed regions were less likely to smoke than those living in remote and underdeveloped regions. Those with lower levels of education and engaging in farm work were also more likely to smoke \(^12\). The urban population’s awareness of the above three diseases caused by smoking was higher than that in rural areas, with significant differences.

To date, most studies of cigarette smoking and mortality have focused on all-aged populations in the US, Australia and Korea \(^13\)\(^8\)\(^14\)\(^15\) with few studies examining the impact of tobacco use on disease and mortality risk among the middle-aged and elderly in China, especially in rural areas. To address this lack of evidence, we aimed to examine the association between smoking status with all-cause mortality among smokers and non-smokers using data from the osteoporosis cohort, which enrolled participants from Anqing, Anhui province, a rural area in Eastern China, in 2003.

**Methods**

**Study design and participants**

This study is part of a large community-based cohort initiated in 2003 among residents of Anhui Province, China \(^16\). The major exclusion criteria included history of type 1 diabetes; renal failure; chronic infections such as tuberculosis or other infectious diseases; malignancies; rickets or other metabolic bone diseases; chronic glucocorticoid use; viral cirrhosis; and thyrotoxicosis.

A total of 18,237 adults participated in the baseline study were re-surveyed with a mean follow-up interval of 14.1 years. 8995 female participants were excluded from this analysis because the number of current and former smokers in the female population was too small to allow for regression analysis. After excluding participants with missing data on smoking status, pack-years of cigarette smoking, family numbers and anyone whose age was below 45 years, the final cohort consisted of 5,367 male participants. All smokers were cigarette smokers.

The study was approved by the Institutional Review Boards of the Anhui Medical University. Written approved informed consent was obtained from each participant. The data supporting the findings of this study will be available from the corresponding author (Xiping Xu) on request.
Death Outcome Collection

Follow-up visits with interviews and data collection were conducted in 2010, 2011, 2014, 2017 and 2018. Data on death was obtained by telephone or face-to-face interviews with participants or household members (if deceased).

Smoking Status, Smoking Intensity, Age of Smoking Initiation and Cessation Age

Smoking status was self-reported by respondents and coded into three categories: current, former, and non-smokers. Current smokers reported smoking more than 10 packs in their lifetime and currently smoke every day or most days. Former smokers reported having smoked 10 packs or more cigarettes in their lifetime but currently have ceased. Non-smokers reported smoking fewer than 10 packs in their entire life. Current smokers were further disaggregated by pack-years\textsuperscript{17} using the equation:

\[
\text{Pack-years} = (\text{Cigarettes per day}/20) \times \text{years smoked}
\]

Pack-years was further divided into three categories (<20, 20–40, ≥40)\textsuperscript{18}, and as a binary variable where it was divided at the median for analysis. We disaggregated former smokers by years since smoking cessation (median), and age of smoking initiation (for current smokers) which was divided into two groups (≤20, and ≥20 years-old).

Statistical Analysis

Means (SD) or medians (25th percentile-75th percentile) and proportions were calculated for population characteristics by smoking status. Differences between groups were achieved with analysis of variance. In the multivariate models, we adjusted for age, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), drinking status, fasting glucose (GLU), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) education level and occupation using Generalized Estimating Equations (GEE) to evaluate the association between baseline smoking status and mortality. Variables in the stratified analysis included BMI (Tertile <20, 20-21.9, ≥20 kg/m\textsuperscript{2}), age (Tertile <51.3, ≥51.3 years), SBP (<130, 130-140, ≥140 mmHg or history of hypertension), DBP (<80, 80-90, ≥90 mmHg or a history of hypertension), and drinking status (never, former, current).

A two-tailed \( P < 0.05 \) was considered statistically significant in all statistical analyses. EmpowerStats (http://www.empowerstats.com) and RStudio software (Version 1.2.5033, http://www.R-project.org/) were used for all statistical analyses.

Results

Study Participants and Baseline Characteristics

Baseline characteristics of the participants according to smoking status (nonsmoker, former smoker and current smoker) are summarized for all males in Table 1. During the 15-year follow-up, the mean ages were 52.3(mean)4.8(SD), 52.5(mean)4.6(SD) and 52.0(mean)4.6(SD) for nonsmokers, former smokers, and current smokers, respectively. We found that current smokers tended to be younger and have lower blood pressure,
body mass index, glucose, total cholesterol and triglycerides levels compared with nonsmokers (Table 1). The results were not similar in women for fewer current smokers. (Supplemental Table 2).

**Effects of Smoking Status on Mortality**

We observed a positive association between baseline pack-years and risk of death (logOR) after adjustment (Figure 1A). Figures 1B and 1C show that younger smoking initiation age and older smoking cessation age were associated with a higher risk of death. The graph displays a decrease in mortality risk as smoking initiation age increases, while as smoking cessation age increases there is an increase in death risk. This finding was further evaluated by GEE models as shown in Table 2. Current cigarette smokers (odds ratio ([OR], 1.60; 95% CI, 1.23,2.08, P<0.001) and former smokers ([OR], 2.12; 95% CI, 1.49,3.01, P<0.001) had higher all-cause mortality risk than non-tobacco users. Relative to nonsmokers, current smokers of fewer than 20 pack-years ([OR], 1.18; 95% CI, 0.85,1.64, P=0.314), 20 to 40 pack-years ([OR], 1.69; 95% CI, 1.28-2.23, P<0.001) and more than 40 pack-years ([OR], 1.85; 95% CI, 1.33,2.56, P<0.001) had a higher all-cause mortality risk.

**Effects of Smoking Initiation Age and Smoking Cessation Age on Mortality**

For smoking initiation age, compared with nonsmokers, current smokers who began smoking before age 20 had a 91% ([OR], 1.91; 95% CI, 1.43,2.54; P<0.001) increased risk for death, and those who began after age 20 ([OR],1.39; 95% CI, 1.06,1.84; P=0.019), had a 39% increased risk of death. The results were consistent across the high and low pack-year groups (Table 3). Those whose smoking cessation age was older than the median age had a 219% ([OR], 3.19; 95% CI, 1.83,5.56; P<0.001) and 116% ([OR], 2.10; 95% CI, 1.21,3.66; P=0.009) increased risk for death in the low vs. high pack-year groups, respectively (Table 4).

**The Joint Effect between Drinking and Smoking on Mortality in Males**

After adjustment, we found that current drinkers who did not smoke had a 42% ([OR], 0.58; 95% CI, 0.32,1.05; P=0.072) decreased risk for death compared to nondrinkers who did not smoke. Those who were both former drinkers and former smokers ([OR], 6.40; 95% CI, 3.03,13.50; P<0.001) had an all-cause mortality risk of more than five times higher than nondrinkers who did not smoke. Regardless of drinking status, the ever-smoking population showed an upward trend in mortality (Table 5). We further performed stratified analyses to assess the effects of smoking status (never, former and current) on death in various subgroups (Supplemental Table 1).

**Discussion**

Our study provides further support that current and former smokers experienced greater risk of death at follow-up than nonsmokers in a Chinese rural population. Younger age at smoking initiation and older age at smoking cessation were both associated with increased risk of mortality.

Risk of all-cause mortality was significantly higher in former or current smokers than in nonsmokers. This finding parallels results from The National Longitudinal Mortality Study. Another study with a mean (SD) follow-up of 6.6 (1.3) years from the National Institutes of Health–AARP Diet and Health Study, showed more powerful evidence. There was a dose-dependent association between reported number of CPD
(cigarettes per day) at baseline with all-cause mortality as well as with deaths from examined smoking-related outcomes. Even those who reported smoking fewer than 1 CPD (HR, 1.99; 95% CI, 1.76, 2.25) or 1 to 10 CPD (HR, 2.60; 95% CI, 2.45, 2.75) had an increased risk of all-cause mortality. Importantly, it extends these findings to show that risk of death associated with smoking remains consistent even for low intensity smoking.

Our study results are striking in that relatively small differences in age at initiation were associated with strong differences in mortality risk 15 years later. A National Health Interview Survey showed that early smoking initiation before age 13 was associated with increased risks for cardiovascular/metabolic (OR:1.67) and pulmonary (OR:1.79) diseases as well as smoking-related cancers (OR:2.1) among current smokers; the risks among former smokers were cardiovascular/metabolic (OR:1.38); pulmonary (OR:1.89); and cancers (OR:1.44). Elevated mortality was also related to early smoking initiation among both current (hazard ratio, 1.18) and former smokers (HR = 1.19). Relative to former smokers, the risk of mortality was lower in individuals who quit smoking at earlier ages. This finding is in agreement with the Sax Institute's 45 and Up Study. Smoking cessation remains beneficial even at age 50. The investigation based on 489,066 participants, aged ≥ 60 years, from 22 population-based cohorts of the CHANCES Consortium confirmed that for former smokers, excess mortality and risk advancement periods (RAPs) decreased with time since cessation, with RAPs of 3.9 (95% CI, 3.0, 4.7), 2.7 (95% CI, 1.8, 3.6), and 0.7 (95% CI, 0.2, 1.1) for those who had quit <10, 10 to 19, and ≥20 years ago, respectively. Similarly, the Zutphen Study found that in 1373 men, stopping cigarette smoking at age 40 increased the life expectancy by 4.6 years, while the number of disease-free life-years was increased by 3.0 years.

To date, most studies about smoke had been focused on urban or general population, only limited studies on smoking and mortality risk have been carried out in Chinese rural areas and in particular none have such a long and large prospective cohort among a male farming population as the current study. Consistently for all these studies, with the increase in pack-years in current smokers, all-cause mortality climbed remarkably. Although the majority of results follow a similar path, our study showed contrary results in former smokers. It is likely that among men who had stopped smoking due to illness, the protective effects of quitting cannot be assessed straightforwardly, even if cessation is substantially protective, because the underlying illness that prompted the smoking cessation may cause a misleadingly elevated risk. The question remains: how does tobacco attribute to all-cause mortality? The "China reported health hazards of smoking" pointed out that tobacco smoke contains 69 known carcinogens, which can cause mutations in key genes, dysregulate normal growth control mechanisms, and eventually lead to the occurrence of cell cancer and malignant tumors. In addition, it also damages vascular endothelial function, which can lead to the occurrence of atherosclerosis, narrowing of the arterial vascular cavity and cause a variety of cardiovascular and cerebrovascular diseases.

Our study has two new findings. Firstly, the age of first tobacco use is an important determinant of mortality risk. Age at smoking initiation was strongly associated with mortality in men over 45 years of age. Ever smokers who started smoking earlier were at a progressively higher risk of mortality during follow-up, relative to those who started smoking later. Similarly, risk of mortality was lower when cessation occurred at an earlier age. This finding supports analogous results abroad. A possible reason is that an earlier age of smoking initiation and a later age of smoking cessation, increases duration of exposure. Secondly, our results suggest that nonsmokers who were ever drinkers, had a potent protective factor for mortality risk in this rural Chinese
population. While, former smokers who were former drinkers were at risk. We surmise that the increase in mortality risk for those who previously used cigarettes and alcohol among this rural population could be a result of stopping usage due to illness.

This study has specific strengths and limitations. Firstly, the data were sparse after stratification, resulting in a larger 95% confidence interval and insignificant results. Secondly, in rural China, smoking cessation was motivated mainly by health issues experienced either directly or indirectly. Nearly all participants who have attempted or successfully quit smoking reported experiencing some health issues prior to quitting. And those who successfully quit frequently reported significant health events that prompted a visit to a doctor\textsuperscript{25}. Lastly, only smoking information collected at baseline was available for this analysis, therefore, it is possible that recall bias existed and some participants who were former smokers at baseline may have resumed smoking afterward, leading to an underestimation of benefits related to smoking cessation. Another weakness of the study was the lack of classification and time of death. Data on smoking-attributable causes of death would have been informative in our interpretation of these results.

**Conclusion**

We provide further evidence that cigarette smoking, regardless of amount, confers significant mortality risks, and that pack-years and age of smoking initiation and cessation, both key components of smoking duration, are important predictors of mortality in Chinese rural adults aged 45 years and older. Younger age at initiation was associated with increased risk of mortality, highlighting the seriousness of the impact that young adult smoking has on lifetime mortality risk. Therefore, smoking cessation incentives and the health benefits of nonsmoking should be promoted and emphasized to youth and all smokers, regardless of age.

**Abbreviations**

\(SBP\) = systolic blood pressure

\(DBP\) = diastolic blood pressure

\(GEE\) = generalized estimating equations

\(BMI\) = body mass index

\(TC\) = total cholesterol

\(TG\) = triglycerides

\(HDL-C\) = high-density lipoprotein cholesterol

\(CI\) = indicates confidence interval

\(OR\) = odds ratio

**Declarations**
**Ethics approval and consent to participate**

The study was approved by the Institutional Review Boards of the Anhui Medical University. Written approved informed consent was obtained from each participant.

**Consent for publication**

Not applicable.

**Availability of data and materials**

The data supporting the findings of this study will be available from the author (Xiping Xu) on request.

**Competing interests**

All authors have completed the ICMJE uniform disclosure form and have declared the following:

Dr. Xiping Xu reports grants from the National Key Research and Development Program [2016YFE0205400, 2018ZX09739010, 2018ZX09301034003], the Science and Technology Program of Guangdong [2020B121202010], the Science and Technology Planning Project of Guangzhou [201707020010], the Science, Technology and Innovation Committee of Shenzhen [GJHS20170314114526143, JSGG20180703155802047], the Economic, Trade and Information Commission of Shenzhen Municipality [20170505161556110, 20170505160926390, 201705051617070].

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**Authors’ contributions**
All authors contributed to the study. Lijing Ye performed the statistical analyses and wrote an initial draft of the paper. Xiping Xu, Binyan Wang, Xiaoshu Cheng and Genfu Tang conceptualized and designed the study, and supervised the survey. Yanfang rong gave guidance on statistical methods. Yue zhang ,Jingyi Li and Nannan Chen performed data and statistical analysis results checking. Other authors supervised and guided the writing of the manuscript. Thank for all authors have provided comments on drafts and contributed to the writing of the manuscript.

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Implications

This study is part of a large community-based cohort initiated in 2003 among residents of Anhui Province, China with a mean follow-up interval of 14.1 years. Among 5,367 male over 45 years, we confirmed that cigarette smoking, regardless of amount, has significant mortality risks, and that pack-years and age of smoking initiation and cessation, are both key components of smoking duration.

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**Tables**

**Table 1. Baseline characteristics of the study participants by smoking status in male**
| Variables                  | Smoking Status     |       |       |       |       |
|---------------------------|--------------------|-------|-------|-------|-------|
|                           | Never (n=990)      | Former (n=528) | Current (n=3849) |
| Age, y                    | 52.3 (4.9)         | 52.5 (4.6)     | 52.0 (4.6)     | 0.023 |
| SBP, mmHg                 | 126.7 (19.8)       | 128.3 (21.2)   | 124.2 (19.6)   | <0.001|
| DBP, mmHg                 | 81.1 (12.0)        | 82.2 (12.6)    | 79.5 (11.9)    | <0.001|
| BMI, kg/m²                | 21.5 (2.6)         | 22.0 (2.8)     | 21.0 (2.4)     | <0.001|
| Laboratory results, mg/dl| Glucose            | 98.5 (91.8, 105.3) | 97.2 (90.7, 104.4) | 96.3 (89.8, 103.5) | <0.001|
|                           | Total cholesterol  | 171.7 (150.0, 192.6) | 172.9 (154.3, 195.0) | 168.0 (148.5, 189.5) | <0.001|
|                           | Triglycerides      | 86.8 (65.5, 119.8) | 89.0 (70.0, 122.7) | 82.4 (62.9, 113.4) | <0.001|
|                           | High density lipoprotein | 53.6 (45.2, 64.3) | 54.5 (45.6, 65.0) | 54.5 (45.2, 65.4) | 0.384 |
| Alcohol Status, No. (%)   | Never              | 670 (67.7)     | 225 (42.6)     | 1947 (50.7)     | <0.001|
|                           | Former              | 17 (1.7)       | 40 (7.6)       | 98 (2.6)        |       |
|                           | Current             | 303 (30.6)     | 263 (49.8)     | 1792 (46.7)     |       |
| Education Level (%)       | Illiterate          | 212 (21.5)     | 114 (21.7)     | 960 (25.0)      | <0.001|
|                           | Elementary school   | 457 (46.4)     | 270 (51.3)     | 1947 (50.8)     |       |
|                           | Middle school and above | 316 (32.1)   | 142 (27.0)     | 928 (24.2)      |       |
| Occupation Type, farmer (%) | 874 (88.4)        | 477 (90.5)     | 3540 (92.1)    | 0.001 |
| History of Hypertension, yes (%) | 62 (6.3) | 48 (9.1) | 146 (3.8) | <0.001 |
| History of Diabetes, yes (%) | 11 (1.1) | 1 (0.2) | 13 (0.3) | 0.004 |

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; SBP, systolic blood pressure. *For continuous variables, values are presented as mean (SD) and mean (SE). Laboratory results are presented as median (IQR).

Table 2. The association between smoking status and mortality in male
| Variables          | N   | Deaths (%) | Crude model | \( P \) value | Adjusted model* | \( P \) value |
|--------------------|-----|------------|-------------|--------------|----------------|--------------|
|                    |     |            | OR (95%CI)  |              | OR (95%CI)     |              |
| **Smoking Status** |     |            |             |              |                |              |
| Never              | 990 | 74 (7.5)   | ref         |              | ref            |              |
| Former             | 528 | 75 (14.2)  | 2.05 (1.46,2.88) | <0.001       | 2.12 (1.49,3.01) | <0.001       |
| Current            | 3849| 430 (11.2) | 1.56 (1.20,2.01) | <0.001       | 1.60 (1.23,2.08) | <0.001       |
| **Pack-years**     |     |            |             |              |                |              |
| Current            |     |            |             |              |                |              |
| <20                | 960 | 82 (8.5)   | 1.16 (0.84,1.60) | 0.378         | 1.18 (0.85,1.64) | 0.314         |
| 20-40              | 2148| 245 (11.4) | 1.59 (1.22,2.09) | <0.001       | 1.69 (1.28,2.23) | <0.001       |
| \( \geq 40 \)     | 741 | 103 (13.9) | 2.00 (1.46,2.74) | <0.001       | 1.85 (1.33,2.56) | <0.001       |

*Adjusted for age, body mass index, systolic blood pressure, diastolic blood pressure, fasting glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol and alcohol drinking status, education level and occupation.

Table 3. The relation of smoking initiation age and pack-years with mortality in current smokers
| N    | Deaths (%) | Crude OR (95%CI) | P value | Adjusted* OR (95%CI) | P value |
|------|------------|------------------|---------|----------------------|---------|
| Never | 990        | 74 (7.5)         | ref     | ref                  |         |
|      |            |                  |         |                      |         |
| Age at smoking initiation, yrs |           |                  |         |                      |         |
| B1($\geq20$) | 2203       | 221 (10)         | 1.38 (1.05,1.81) | 0.020 | 1.39 (1.06,1.84) | 0.019 |
| B2(<20) | 1646       | 209 (12.7)       | 1.80 (1.36,2.38) | <0.001 | 1.91 (1.43,2.54) | <0.001 |
| Pack-years(<20) |           |                  |         |                      |         |
| $\geq20$ | 697        | 59 (8.5)         | 1.14 (0.81,1.63) | 0.452 | 1.22 (0.85,1.75) | 0.279 |
| <20   | 263        | 23 (8.7)         | 1.19 (0.73,1.93) | 0.491 | 1.26 (0.76,2.08) | 0.378 |
| Pack-years(20-40) |           |                  |         |                      |         |
| $\geq20$ | 1230       | 130 (10.6)       | 1.46 (1.09,1.97) | 0.012 | 1.50 (1.11,2.04) | 0.009 |
| <20   | 918        | 115 (12.5)       | 1.77 (1.30,2.41) | <0.001 | 1.98 (1.43,2.74) | <0.001 |
| Pack-years($\geq40$) |           |                  |         |                      |         |
| $\geq20$ | 276        | 32 (11.6)        | 1.62 (1.05,2.51) | 0.030 | 1.42 (0.90,2.23) | 0.132 |
| <20   | 465        | 71 (15.3)        | 2.23 (1.58,3.14) | <0.001 | 2.13 (1.49,3.06) | <0.001 |

*Adjusted for age, body mass index, systolic blood pressure, diastolic blood pressure, fasting glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol and alcohol drinking status, education level and occupation.

**Table 4. The relation of smoking cessation age and pack-years with mortality in former smoker**
| Smoking Status | N   | Deaths (%) | Crude OR (95%CI) | Adjusted* OR (95%CI) | P value | P value |
|----------------|-----|------------|------------------|----------------------|---------|---------|
| Never          | 990 | 74 (7.5)   | ref              | ref                  |         |         |
| Age at cessation, yrs |       |            |                  |                      |         |         |
| B1(<46)        | 255 | 31 (12.2)  | 1.71 (1.09,2.68) | 2.43 (1.49,3.96)     | 0.018   | <0.001  |
| B2(≥46)        | 273 | 44 (16.1)  | 2.38 (1.60,3.54) | 2.22 (1.45,3.41)     | <0.001  | <0.001  |
| pack-years (<median(26)) |       |            |                  |                      |         |         |
| B1(<41)        | 126 | 13 (10.3)  | 1.42 (0.76,2.66) | 2.28 (1.17,4.45)     | 0.267   | 0.016   |
| B2(≥41)        | 130 | 23 (17.7)  | 2.66 (1.60,4.44) | 3.19 (1.83,5.56)     | <0.001  | <0.001  |
| pack-years (≥median(26)) |       |            |                  |                      |         |         |
| B1(<49)        | 135 | 16 (11.9)  | 1.66 (0.94,2.96) | 2.06 (1.10,3.84)     | 0.083   | 0.024   |
| B2(≥49)        | 137 | 23 (16.8)  | 2.50 (1.51,4.13) | 2.10 (1.21,3.66)     | <0.001  | 0.009   |

*Adjusted for age, body mass index, systolic blood pressure, diastolic blood pressure, fasting glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol and alcohol drinking status, education level and occupation.

Table 5. The joint effect between drinking and smoking on mortality in males

| Drinking Status | Smoking Status | Never | Former | Current |
|-----------------|----------------|-------|--------|---------|
|                 | Deaths (%)    | OR (95%CI) | Deaths (%) | OR (95%CI) | Deaths (%) | OR (95%CI) |
| Never           | 58 (8.7)      | Ref   | 35 (15.6) | 2.18 (1.37, 3.48) | 204 (10.5) | 1.31 (0.95, 1.80) |
| Former          | 1 (5.9)       | 0.66 (0.09, 4.65) | 14 (35.0) | 6.40 (3.03,13.50) | 22 (22.4) | 2.56 (1.47, 4.47) |
| Current         | 15 (5)        | 0.58 (0.32, 1.05) | 26 (9.9) | 1.23 (0.74, 2.04) | 203 (11.3) | 1.39 (1.00, 1.93) |

P for interaction = 0.034
Adjusted for age, body mass index, systolic blood pressure, diastolic blood pressure, fasting glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol, alcohol drinking status, education level and occupation.

**Figures**

**Figure 1**

Smooth curves between smoking status and death.

**Supplementary Files**

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- Supplementalfigureflowchart.tif
- SupplementalTable.docx