Effects of smoking intensity trajectory, cumulative smoking exposure, and the number of years since quitting on the subsequent risk of hypertension

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Abstract
The aim of this study was to investigate the effects of smoking intensity trajectory, cumulative smoking exposure, and the number of years since quitting on the subsequent risk of hypertension in Chinese adults. The study included 2783 men and 3416 women who participated in at least three waves of the China Health and Nutrition Survey. Information regarding smoking behavior was obtained using a standardized questionnaire. The trajectory of smoking intensity was determined using a group-based trajectory model. The number of pack-years of smoking and the number of years since quitting were calculated. The incidence of hypertension was 18.2% and 15.5% in men and women, respectively, during a median follow-up duration of 4 years. Male participants with trajectories denoting light and moderate smoking had increased risks of hypertension compared with those with trajectories denoting non-smoking (P < .05). Compared with male participants with 0 pack-years, those with < 5.5 pack-years had a higher risk of hypertension (P < .05). Male participants with ≥ 5.5 pack-years and weight gain had a higher risk of hypertension compared with those with 0 pack-years and weight loss (P < .05). However, smoking was not related to an increased risk of hypertension in women. Additionally, similar to never smoking, having quit within 2–5 years or ≥ 5 years was not associated with the incidence of hypertension in men. The results of this study showed that light/moderate smoking or high cumulative smoking exposure accompanied by weight gain increased the risk of hypertension in Chinese men and smoking cessation decreased this effect.

KEYWORDS
hypertension, smoking, trajectories

1 | INTRODUCTION

Tobacco use is a major public health concern.1 It damages almost every organ system and leads to adverse health consequences, such as cardiovascular diseases.2 Smokers tend to suffer from premature death, with some studies showing that smokers live 10 years less than individuals who have never smoked.2 Globally, 8 million deaths are attributable to tobacco use annually.2
China accounts for more than one third of global tobacco consumption, and the 341 million tobacco smokers in China account for approximately 30% of the world’s tobacco-smoking population. Previous studies have shown that the prevalence of smoking is extremely high in Chinese men, but low in Chinese women. This is in contrast to findings from other countries, where a high prevalence of smoking has been documented in the female population. Therefore, the adverse health effects attributable to tobacco use in Chinese men and women need to be clarified.

Hypertension and its associated diseases are a major public health concern in China. A previous study reported a high prevalence of hypertension in China, but a low level of awareness and poor treatment and control measures. Primary prevention is the key to preventing and controlling hypertension and its associated diseases. Cross-sectional studies have not previously been able to determine whether there is an association between smoking and hypertension. Previous cohort studies have measured smoking status at only one time and have not considered the trajectory of smoking status over time. Therefore, a cohort study based on multiple follow-up visits is needed to better assess the effect of the smoking status trajectory over time on the incidence of hypertension. Additionally, evidence regarding the cumulative effects of smoking exposure and the number of years since quitting on the incidence of hypertension is limited in China. In this study, we used data collected from the China Health and Nutrition Survey (CHNS) to address the aforementioned issues.

2 | MATERIALS AND METHODS

2.1 | Study population

The CHNS is an open, continuous, and population-based longitudinal study that was launched in 1989 by the University of North Carolina at Chapel Hill and the National Institute of Nutrition and Food Safety of the Chinese Center for Disease Control and Prevention. Ten survey waves were conducted at either 2- or 4-year intervals from the launch of the CHNS until 2015. Details of the design and implementation procedures of the CHNS study have been reported elsewhere. Briefly, a process involving multistage random clustering was used to obtain the study sample. A questionnaire survey was then administered, and anthropometric data (blood pressure [BP]) were collected in each survey wave. The CHNS was approved by the institutional review boards of the University of North Carolina at Chapel Hill and the Institute of Nutrition and Health of the Chinese Center for Disease Control and Prevention. All participants provided written informed consent.

Individuals were deemed eligible for the present study if they (1) participated in at least three survey waves; (2) were ≥18 years old at the time of completing their first survey; (3) provided complete and accurate information about their smoking behavior, BP, weight, height, sex, and age; and (4) were healthy and not pregnant (n = 10 776). Participants who were diagnosed with hypertension before completing the final survey were excluded (n = 4577). Thus, the study sample comprised 6,199 participants. The study design is described in Figure S1.

2.2 | Primary exposure

Information about the participants’ smoking behavior was collected using the survey questionnaire during each survey wave. The participants were classified as either current smokers or current non-smokers according to their smoking status at the time of the given survey. Current smokers answered the following question: “How many cigarettes do you smoke per day?” The participants’ answers to this question were used to determine smoking intensity.

The pack-years metric was used to represent cumulative smoking exposure. Pack-years was calculated by multiplying the number of packs of cigarettes smoked per day (calculated by dividing the number of cigarettes smoked per day by 20) by the number of years of smoking. After excluding male participants with 0 pack-years, the median number of pack-years was 5.5. The male participants were then divided into “0,” “<5.5,” and “≥5.5” pack-years groups. Female participants were divided into “0” and “≥0” pack-years groups due to the relatively low number of female smokers included in the study.

Because the number of female smokers was low, we only analyzed the association between the number of years since quitting and hypertension in men. Male participants who responded that they never smoked from the first to the (N-1) surveys were included in the “never smoker” group; those who responded that they smoked in the (N-1) survey were included in the “current smoker” group and those who smoked prior to the (N-1) survey, but did not smoke at the time of the (N-1) survey, were included in the “former smoker” group. The number of years since quitting was calculated for male former smokers. After excluding those with 0 years since quitting, 5 years was the median and 2 years was the minimum time since quitting. Consequently, male participants were classified into “never smoker,” “current smoker,” “former smoker with 0 years since quitting,” “former smoker with 2-5 years since quitting,” and “former smoker with ≥5 years since quitting” groups.

2.3 | Outcome ascertainment

During each survey wave, after the participants were allowed 10 min of seated rest, trained workers used a standard mercury sphygmomanometer with an appropriate cuff size to measure BP on the right arm. BP was measured three times and the mean value was used for analysis. We defined participants as hypertension if they had a systolic BP of ≥ 140 mmHg, or a diastolic BP of ≥ 90 mmHg, or they used antihypertensive drugs.

2.4 | Covariate assessment

Participants’ heights and weights were measured and body mass index (BMI) was calculated. Participants with a BMI ≥ 24 kg/m² were
RESULTS

Statistical analysis using a group-based trajectory model.22 We used a censored normal exposure groups, or number of years since quitting groups. Different smoking intensity trajectory groups, cumulative smoking exposure and the number of years since quitting on the subsequent risk of hypertension, we used covariate-adjusted Poisson models with robust standard errors to calculate relative risks (RRs) and 95% confidence intervals (CIs).25 Model 1 was adjusted for the length of follow-up and characteristic on the (N-1) survey (age, drinking, Han nationality, urban residence, completed upper middle school and above, marital status, household asset score, leisure physical activity, fat intake, systolic BP, diastolic BP, and overweight/obesity defined by BMI). In model 2, we retained all of the covariables, except for overweight/obesity defined by BMI, which we replaced with weight change. Given the interaction between smoking and weight status, participants were classified into several groups based on the combination of smoking status and weight change.

To evaluate the robustness of the results, we performed sensitivity analyses by repeating the aforementioned analyses after adjusting for pre-central obesity/central obesity defined by WC.

We used SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA) for data analyses. All of the P-values were two-sided, and a P-value below .05 was considered statistically significant.

3 | RESULTS

Table 1 shows the characteristics of the male and female participants at the first survey. In total, 2783 men and 3416 women (mean age: 34.7 vs 35.8 years; mean systolic BP: 112.0 vs 107.6 mmHg; mean diastolic BP: 73.0 vs 70.4 mmHg; mean BMI: 21.3 vs 21.6 kg/m²; all P < .001) were included in this study. The smoking prevalence at the first survey was 62.3% and 3.3% for male and female participants, respectively (P < .001). The median number of cigarettes smoked per day at the first survey was 8 and 0 for male and female participants, respectively (P < .001). Table S1 summarizes the characteristics of the male and female participants who completed the (N-1) survey. Of those who took part in the (N-1) survey, male participants tended to be younger, consume more alcohol, and have a higher educational level than female participants. The incidence of hypertension was 18.2% and 15.5% for men and women, respectively, during a median follow-up duration of 4 years from the (N-1) to the N survey.

Table 2 presents the associations of the trajectory of the number of cigarettes smoked per day across age with the incidence of hypertension. In males, the incidence of hypertension was 13.6%, 19.9%, 19.3%, and 23.2% in the non-smoking, light smoking, moderate smoking and heavy smoking groups (P = .003), respectively, whereas in females, the incidence of hypertension was 15.3% and 19.7% in the non-smoking and smoking groups (P = .149), respectively. In model 1, after adjusting for covariates, compared with males in the non-smoking group, those in the light smoking (RR [95% CI]: 1.33 [1.02–1.72]) and moderate smoking (RR [95% CI]: 1.36 [1.10–1.68]) groups had a significantly higher risk of hypertension, whereas those in the heavy smoking...
TABLE 1 Characteristics of participants on first survey stratified by gender

|                | Males | Females | P  |
|----------------|-------|---------|----|
| No.            | 2783  | 3416    |    |
| Age, years     | 34.7±12.7 | 35.8±12.1 | <.001 |
| Han Nationality, no. (%) | 2381 (85.6) | 2958 (86.6) | .240 |
| Urban residence, no (%) | 874 (31.4) | 1185 (34.7) | .006 |
| Completed Upper middle school and above, no. (%) | 708 (25.4) | 691 (20.2) | <.001 |
| Marital status, no. (%) | <.001  |         |    |
| Never married  | 705 (25.3) | 247 (7.2) |    |
| Married        | 2029 (72.9) | 3033 (88.8) |    |
| Divorced/Separated/Widowed | 49 (1.8) | 136 (4.0) |    |
| Drinking, no. (%) | 1683 (60.5) | 369 (10.8) | <.001 |
| Leisure physical activity, no. (%) | 74 (2.7) | 60 (1.8) | .015 |
| Fat intake, g/day | 65.8 (47.9) | 58.5 (42.7) | <.001 |
| Body mass index, kg/m² | 21.3±2.5 | 21.6±2.8 | <.001 |
| Overweight/obesity, no. (%) | 369 (13.3) | 635 (18.6) | <.001 |
| Household asset score | 2.0 (2.0) | 2.0 (3.0) | <.001 |
| SBP, mmHg | 112.0±10.7 | 107.6±11.6 | <.001 |
| DBP, mmHg | 73.0±7.9 | 70.4±8.5 | <.001 |

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Data were presented as means ± SDs, median (interquartile range) and number (%) for normal and non-normal continuous variables and categorical variables, respectively.

Differences between groups were compared using the chi-square test, Wilcoxon rank sum test, or t-test.

TABLE 2 Association of trajectories of number of cigarettes smoking per day across age with incidence of hypertension

|                | No. | Prevalence, % | Model 1a | Model 2b |
|----------------|-----|---------------|----------|----------|
|                |     |               | RR (95% CI) | P       | RR (95% CI) | P       |
| Men            |     |               |          |         |          |         |
| Non-smoking    | 692 | 13.6          | Ref      |         | Ref      |         |
| Light smoking  | 448 | 19.9          | 1.33 (1.02, 1.72) | .032 | 1.34 (1.03, 1.74) | .028 |
| Moderate smoking | 1531 | 19.3 | 1.36 (1.10, 1.68) | .004 | 1.33 (1.08, 1.64) | .008 |
| Heavy smoking  | 112 | 23.2          | 1.32 (0.92, 1.90) | .129 | 1.31 (0.91, 1.89) | .150 |
| Women          |     |               |          |         |          |         |
| Non-smoking    | 3269 | 15.3         | Ref      |         | Ref      |         |
| Smoking        | 147  | 19.7          | 0.78 (0.55, 1.10) | .155 | 0.80 (0.57, 1.13) | .210 |

CI, confidence interval; RR, risk ratio.

Model 1 was adjusted for the length of follow-up and characteristic on (N-1) survey (age, drinking, Han nationality, urban residence, completed upper middle school and above, marital status, household asset score, leisure physical activity, fat intake, systolic blood pressure, diastolic blood pressure, and overweight/obesity).

Model 2 was adjusted for the length of follow-up, characteristic on (N-1) survey (age, drinking, Han nationality, urban residence, completed upper middle school and above, marital status, household asset score, leisure physical activity, fat intake, systolic blood pressure, and diastolic blood pressure), and weight change from (N-1) to first survey.
## TABLE 3
Association of cumulative pack-years of smoking with incidence of hypertension

| No. | Prevalence, % | Model 1<sup>a</sup> | Model 2<sup>b</sup> |
|-----|---------------|----------------------|----------------------|
|     |               | RR (95% CI)          | P                    | RR (95% CI)          | P                    |
| Men, pack-years |   |                      |                      |                      |
| 0   | 761           | 13.9                 | Ref                  | Ref                  |
| <5.5<sup>c</sup> | 1004           | 19.1                 | 1.30 (1.05, 1.60)    | .017                 | 1.29 (1.04, 1.59)    | .020                 |
| ≥5.5<sup>c</sup> | 1018           | 20.3                 | 1.19 (0.96, 1.47)    | .109                 | 1.17 (0.94, 1.45)    | .153                 |
| Women, pack-years |   |                      |                      |                      |
| 0   | 3269          | 15.3                 | Ref                  | Ref                  |
| >0  | 147           | 21.1                 | 0.83 (0.59, 1.17)    | .283                 | 0.86 (0.61, 1.20)    | .370                 |

CI, confidence interval; RR, risk ratio.
<sup>a</sup>Model 1 was adjusted for the length of follow-up and characteristic on (N-1) survey (age, drinking, Han nationality, urban residence, completed upper middle school and above, marital status, household asset score, leisure physical activity, fat intake, systolic blood pressure, diastolic blood pressure, and overweight/obesity).
<sup>b</sup>Model 2 was adjusted for the length of follow-up, characteristic on (N-1) survey (age, drinking, Han nationality, urban residence, completed upper middle school and above, marital status, household asset score, leisure physical activity, fat intake, systolic blood pressure, and diastolic blood pressure), and weight change from (N-1) to first survey.
<sup>c</sup>5.5 was median after excluding the male participants with 0 pack-years.

## TABLE 4
Association of years since quitting with incidence of hypertension in Chinese men

| No. | Prevalence, % | Model 1<sup>a</sup> | Model 2<sup>b</sup> |
|-----|---------------|----------------------|----------------------|
|     |               | RR (95% CI)          | P                    | RR (95% CI)          | P                    |
| Never smoker |   |                      |                      |                      |
| 613           | 12.9                 | Ref                  | Ref                  |
| Current Smoker | 1667             | 18.9                 | 1.37 (1.10, 1.72)    | .006                 | 1.35 (1.07, 1.69)    | .010                 |
| Former Smoker, years since quitting |     |                      |                      |                      |
| 0 years since quitting | 280           | 21.4                 | 1.52 (1.13, 2.04)    | .005                 | 1.51 (1.12, 2.02)    | .007                 |
| 2–5 years<sup>c</sup> | 96           | 19.8                 | 1.25 (0.80, 1.95)    | .331                 | 1.27 (0.81, 1.98)    | .304                 |
| ≥5 years<sup>c</sup> | 127           | 25.2                 | 1.42 (0.99, 2.02)    | .055                 | 1.43 (1.00, 2.04)    | .051                 |

CI, confidence interval; RR, risk ratio.
<sup>a</sup>Model 1 was adjusted for the length of follow-up and characteristic on (N-1) survey (age, drinking, Han nationality, urban residence, completed upper middle school and above, marital status, household asset score, leisure physical activity, fat intake, systolic blood pressure, diastolic blood pressure, and overweight/obesity).
<sup>b</sup>Model 2 was adjusted for the length of follow-up, characteristic on (N-1) survey (age, drinking, Han nationality, urban residence, completed upper middle school and above, marital status, household asset score, leisure physical activity, fat intake, systolic blood pressure, and diastolic blood pressure), and weight change from (N-1) to first survey.
<sup>c</sup>5 was median after excluding the male former smoker with 0 years since quitting; 2 was minimum value after excluding the male former smoker with 0 years since quitting.

The incidence of hypertension was 12.9%, 18.9%, 21.4%, 19.8%, and 25.2% in male participants in the never smoker, current smoker, former smoker with 0 years since quitting, former smoker with 2–5 years since quitting, and former smoker with ≥5 years since quitting groups (P = .001), respectively. In model 1, after adjusting for covariates, compared with never-smokers, current smokers (RR [95% CI]: 1.37 [1.10–1.72]) and former smokers with 0 years since quitting (RR [95% CI]: 1.52 [1.13–2.04]) had higher risks of hypertension; however, former smokers with 2–5 years since quitting and former smokers with ≥5 years since quitting had similar risks of hypertension (P< .05).

In model 2, the above-mentioned results did not change significantly.

We performed sensitivity analyses after adjusting for pre-central obesity /central obesity defined by WC and obtained similar results (Table S7–S9).

4 | DISCUSSION

In this nationwide population-based longitudinal study, we observed that male participants with trajectories denoting light smoking or...
moderate smoking had increased risks of hypertension. We also confirmed that male participants with < 5.5 pack-years had a higher risk of hypertension than those with 0 pack-years. Further, we found that the risk of hypertension was similar between Chinese men who never smoked and those who were former smokers, but quit within 2–5 or ≥5 years. Additionally, male participants in ≥5.5 pack-years and weight gain group had a higher risk of hypertension than those in the 0 pack-years and weight loss group. However, smoking was not associated with an increased risk of hypertension in Chinese women.

We used multiple follow-up visits to collect additional information, which showed that distinct smoking intensity trajectories conferred significantly different risks of hypertension in Chinese men. Male participants with trajectories denoting light smoking and moderate smoking had increased risks of hypertension compared with those with trajectories denoting non-smoking. Our findings are partly supported by previous studies showing a significant association between smoking and elevated BP. A cohort study in Indonesia found a significant effect of changes in smoking status on BP, which is consistent with the results of our present study. A cross-sectional study in a Chinese male population suggested that smoking is associated with increased odds of masked daytime ambulatory hypertension and hypertension at home in the evening. Smoking has also been shown to contribute to the incidence of hypertension by increasing arterial stiffness and sympathetic nervous system activation.

The results of this study also suggested that male participants with < 5.5 pack-years of smoking had an increased risk of hypertension than those without cumulative smoking exposure. A cohort study in Hispanic adults reported a similar effect of cumulative smoking exposure on the incidence of hypertension. Similarly, a cross-sectional study in China showed that smoking duration was positively associated with systolic BP.

Our findings indicated that male former smokers with 2–5 years and ≥5 years since quitting had similar risks of hypertension relative to never smokers. In line with the findings of the current study, a previous study found that the effect of smoking on increased aortic stiffness was reversible after smoking cessation. The CARDIA longitudinal study pointed out that systolic BP and diastolic BP did not differ between long-term former smokers and never smokers. However, a 4-year follow-up study in Korean men reported that smoking cessation results in hypertension. These contradictory findings may be attributable to variations in the characteristics of the study populations, study outcomes, sample sizes, number of BP measurements and number of follow-up visits. A randomized crossover design trial reported that quitting smoking after a short period of time decreased ambulatory BP in male habitual smokers, which partly aligns with the findings of the present study.

Unexpectedly, male participants in ≥5.5 pack-years did not have higher risk of hypertension compared with those in 0 pack-years. The reason may be attributed to small effect of smoking on hypertension, as described in previous studies. Future studies with large sample size were needed to analyze the association of cumulative smoking exposure with hypertension. Previous studies have reported that heavy smoking is related to an increased risk of obesity. Our study also showed that male participants with ≥5.5 pack-years of smoking tended to gain weight. This finding may be attributed to the clustering of risky behaviors in heavy smokers. Consequently, the combined effect of smoking and these risky behaviors on hypertension should be considered. This study contributed valuable information to the field by showing that the male participants in ≥5.5 pack-years and weight gain group had a higher risk of hypertension than those in the 0 pack-years and weight loss group. Additionally, our finding showing that male participants who quit smoking tended to gain weight was consistent with the findings of previous studies (Table S6). This study showed that male former smokers with a longer time since quitting and with weight gain were more likely to have hypertension in comparison with never smokers.

We found no significant effect of smoking on the risk of hypertension in Chinese women. A previous cohort study also indicated that cotinine-verified smoking was non-significantly associated with incident hypertension in Korean women. Similarly, the CARDIA longitudinal study demonstrated that systolic BP did not differ between consistent smoker and never smokers among Black or White women. This may be attributed to less individual cumulative smoking exposure in women, which may not be sufficient to cause the onset of hypertension. The Health Survey for England also reported a small effect of smoking on BP, indicating that sufficient cumulative smoking exposure may be required to induce hypertension. Sex discrepancies in the association between smoking and hypertension may also be due to complex interrelationships between smoking and other covariates. A previous study demonstrated an association between passive smoking and hypertension in non-smoking elderly Chinese women. Moreover, the adverse health outcomes of smoking have been well-documented in women.

The present study has some limitations. First, the self-reporting of information about smoking behavior may have limited the accuracy of such information. A previous study showed the difference in self-reported and cotinine-verified smoking status. Second, the effect of e-cigarette use on hypertension could not be analyzed due to the lack of relevant information. Third, the relatively low numbers of male heavy smokers, male former smokers, and female smokers included in the study may have introduced the bias. Additional studies are warranted to investigate the relationship between smoking and hypertension in Chinese adults. Fourth, we did not adjust for weight change defined by WC due to missing data in the first survey (eg, only 1428 of the 2783 male participants had weight change data defined by WC). Finally, when calculating the number of pack-years and number of years since quitting, we assumed that an individual’s smoking behavior was carried forward from a given examination (ie, examination 2) and did not change until a different status was recorded at a subsequent examination (ie, examination 3). This approach may have introduced bias.

The results of this study showed that light/moderate smoking or high cumulative smoking exposure and weight gain increased the risk of hypertension in Chinese men and smoking cessation decreased this effect.
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CONFLICT OF INTEREST
The authors report no conflict of interest.

AUTHOR CONTRIBUTIONS
HF conceptualized and designed the study, carried out the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript; XYZ critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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SUPPORTING INFORMATION
Additional supporting information can be found online in the Supporting Information section at the end of this article.

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