ABSTRACT

Background: Increasing number of studies have suggested the time to first cigarette after waking (TTFC) have significant positive effect on respiratory diseases. However, few of them focused on the Chinese population. This study aims to estimate the impact of TTFC on the prevalence of chronic respiratory diseases (CRD) in Chinese elderly and explore the association in different sub-populations.

Methods: Cross-sectional data of demographic characteristics, living environment, smoking-related variables, and CRD were drawn from the Chinese Longitudinal Healthy Longevity Survey in 2018. Multivariate stepwise logistic regression analyses were conducted to examine the association of the TTFC with the prevalence of CRD.

Results: This study includes 13,208 subjects aged 52 years and older, with a mean age of 85.3 years. Of them, 3,779 participants were ex- or current smokers (44.9% had the TTFC ≤30 minutes, 55.1% >30 minutes) and 1,492 had suffered from CRD. Compared with non-smokers, participants with TTFC ≤30 minutes seemed to have higher prevalence of CRD (OR 1.97; 95% CI, 1.65–2.35) than those with TTFC >30 minutes (OR 1.70; 95% CI, 1.44–2.00), although the difference was statistically insignificant (Pinteraction = 0.12). Compared with TTFC >30 minutes, TTFC ≤30 minutes could drive a higher prevalence of CRD among female participants, those aged 90 years and older, urban residents, and ex-smokers (Pinteraction < 0.05).

Conclusion: Shorter TTFC relates to higher prevalences of CRD in Chinese older females, those aged 90 years and older, urban residents, and ex-smokers. Delaying TTFC might partially reduce its detrimental impact on respiratory disease in these specific subpopulations.

Key words: time to first morning cigarette; chronic respiratory diseases; Chinese elderly; Chinese Longitudinal Healthy Longevity Survey

INTRODUCTION

Respiratory disease is an umbrella term that includes bronchitis, emphysema, asthma, and pneumonia, and it is associated with significant morbidity and mortality among the older population. Smoking has been determined as one of the leading risk factors of respiratory disease. In addition to the traditional predictor valuates of smoking intensity and consumption duration, the time to first cigarette after waking (TTFC) has been suggested as a novel proxy of nicotine dependence and could be more valuable in precisely assessing smokers’ risk of respiratory disease. For example, people with a shorter TTFC have a higher risk of asthma, chronic obstructive pulmonary disease, and lung cancer. Therefore, there are great disparities in smoking pattern among smokers with various sociocultural backgrounds and genetic phenotypes, which might be responsible for ethnic disparities in smoking-related health consequences. While a number of existing studies only focused on the relationship between the TTFC and the risk of respiratory disease among specific population, rather than comprehensive subgroup analyses across sub-populations of smokers (such as those stratified by gender, age, smoking status), so it has limited the application of study findings to some extent. Considering that smokers today are increasingly likely to have their first cigarette earlier on awakening than they were a decade ago, national studies are warranted to explore heterogeneity within ethnic groups or sub-populations.

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With the population aging worldwide, global burden of late-life disease has steadily increased and smoking-related diseases were one of outstanding challenges of them. About 167 million Chinese, accounting for 11.9% of the total population, were 65 years and older at the end of 2018, and the aging is accelerating. Furthermore, with lung function decline, such as loss of lung elasticity and reduced thoracic cage movement, the prevalence of respiratory diseases are high among the elderly comparing to the youth. The TTFC has been identified as a valid indicator for the risk of respiratory disease in Europeans and Americans; however, no study has been conducted to examine the relationship between the TTFC and the risk of respiratory disease of China’s elderly population yet. With the data of the Chinese Longitudinal Healthy Longevity Survey (CLHLS), this study aims to investigate the association between the TTFC and the prevalence of chronic respiratory diseases (CRD) among the Chinese elderly people and further explore the association in different sub-populations.

**METHODS**

**Study design and participants**

The CLHLS is an ongoing, prospective, and national study of community-dwelling Chinese older people started from 1998, and follow-up interview was performed every 2 to 3 years. The rationale, design and methods of this survey have been previously described in detail. Briefly, this survey includes about 16,000 elderly people from more than 500 sample points in 22 province-level administrative regions across China. The surveys are administered in participants’ homes by trained interviewers with a structured questionnaire. Proxy respondents, usually a spouse or other close family members, are interviewed when participants are unable to answer questions. In this study, we interviewed all participants (n = 15,874) enrolled in the latest wave of the survey in 2018. After excluding 802 questionnaires with missing data of exposure (the TTFC) and 1,864 with missing data of CRD (suffering from bronchitis/emphysema/asthma/pneumonia or not), 13,208 respondents were ultimately included as study population, yielding a qualification rate of 83.2% (Figure 1).

The CLHLS was approved by the Research Ethics Committee of Peking University (IRB00001052-13074), and all participants or their proxy respondents provided written informed consent.

**Data collection**

The TTFC was measured based on smoker’s answer to the question of “How soon do you smoke your first cigarette after you wake up?”. Then, we dichotomized the TTFC into two groups: ≤30 minutes and >30 minutes. Smoking status were recorded and divided into three categories (never, ex-, and current) according to the questionnaire. The outcome (the prevalence of respiratory disease) in this study was defined based on a yes or no answer to the question of “Are you suffering from bronchitis/emphysema/asthma/pneumonia that has been diagnosed?”

We further collected information of participants from following four domains: 1) demographic characteristics (eg, sex, age, rurality, years of schooling, marital status, body mass index [BMI; underweight: BMI <18.5 kg/m²; normal weight: BMI 18.5–23.9 kg/m²; overweight/obesity: BMI ≥24.0 kg/m²]; 2) lifestyle factors (eg, alcohol consumption, physical exercise [referring to purposeful fitness activities, such as walking, playing ball, running, and qigong], sleep time); 3) household environment (eg, walking time to the nearest medical institution, distance to the arterial road, fuel of cooking, ventilation of kitchen, air cleaning in household, living expenses); 4) smoking related factors (eg, past-present smoking status, smoking times per day, years of smoking, smoking amount per day of housemates). For the covariates with missing values of no more than 5%, we used the multiple imputation to replace the missing data with one or more specific values, results were combined using the standard rules from Rubin. Finally, only a small percentage of the data for most covariates were missing (<2%), with the exception of fuel for cooking (3.8%) and ventilation of the kitchen (4.5%).
Statistical analysis
Data of the survey were inputted into the SPSS software (Version 22.0, SPSS Inc, Chicago, IL, USA) for statistical analyses. Continuous variables were described as mean (standard deviation [SD]), and frequency data were expressed as number (%). We analyzed the demographic statistics using the χ² test. Forward stepwise multivariate logistic regression analysis (level for selection: P ≤ 0.05, level for elimination: P ≥ 0.10) were used to estimate the association between the TTFC and prevalence of CRD among the Chinese elder people, with non-smokers as the reference group. We also tested the statistical significance of the difference of the estimates.24

We did several sensitivity analyses (models 2–7), where we added different covariates into model 1, to examine the robustness of the primary results. In model 2, we controlled only for age and sex. In model 3–5, we added covariates mentioned above into models step-by-step. In model 6, we controlled only past-present smoking status and smoking amount per day. In model 7, we included all covariates. Furthermore, we also did subgroup analyses stratified by sex, age, rurality, past-present smoking status and smoking amount per day, respectively, to study the impact of TTFC on CRD in different sub-populations. The significance level was accepted as P < 0.05 (two-sided) for all tests.

RESULTS
We included 13,208 participants in this study. The mean age was 85.3 (SD, 11.7) years old, and 7,456 (56.5%) participants were female. Over a quarter (28.6%) of participants reported smoking. Of them, 1,747 respondents (46.2%) were ex-smokers, and 2,013 respondents (53.8%) were current smokers; 1,695 respondents (44.9%) had the TTFC ≤30 minutes, 2,084 respondents (55.1%) reported the TTFC >30 minutes; 2,027 respondents (53.6%) smoked ≤10 times per day, and 1,752 respondents (46.4%) smoked >10 times per day. A total of 1,492 (11.3%) respondents have suffered from the CRD (Table 1).

Univariate analysis (Table 1) shows that sex, age, rurality, alcohol consumption, sleep time, ventilation of kitchen, distance to the nearest medical institution, fuels of cooking, distance to the arterial road, past-present smoking status, smoking times per day, years of smoking, and smoking amount of housemates were all significantly associated with the prevalence of CRD (P < 0.05). Table 2 shows that the association between the TTFC and the prevalence of CRD through forward stepwise multivariable logistic regression analyses. Compared with non-smokers, respondents with the TTFC ≤30 minutes were 1.97 times more likely to report prevalence of CRD (OR 1.97; 95% CI, 1.65–2.35), while respondents with TTFC >30 minutes were 1.70 times more (OR 1.70; 95% CI, 1.44–2.00). However, the difference between two estimates was statistically insignificant (Pinteraction = 0.12). The association of TTFC and the prevalence of CRD remained significant after adjusting for demographic characteristics and other covariates (eTable 1, eTable 2, eTable 3, eTable 4, eTable 5, and eTable 6). In subgroup analyses, the effect of the TTFC on the prevalence of CRD was significantly different by sex, age, rurality, past-present smoking status, or smoking amount per day. In the female group, compared with those who had the TTFC >30 minutes, respondents with the TTFC ≤30 minutes shown significantly higher prevalence of CRD (3.06 vs 1.82). Similar results were also found among respondents aged 90 years and older (1.92 vs 1.43), urban residents (2.62 vs 1.64), and those ex-smokers (2.54 vs 1.95) (all Pinteraction < 0.05). (Figure 2 and eTable 8, eTable 9, eTable 10, eTable 11, and eTable 12).

DISCUSSION
This study has presented a comprehensive analysis on the association between the TTFC and the prevalence of CRD among older Chinese population using a large scale national representative sample. We found both the shorter (≤30 minutes) and longer (>30 minutes) TTFC were positively associated with the prevalence of CRD among the Chinese elderly, but there was no statistically significant difference between the two estimates. This finding was inconsistent with that of previous studies conducted in other countries.6,9,10,25 However, compared with TTFC >30 minutes, TTFC ≤30 minutes could significantly increase the prevalence of CRD among females, individuals aged 90 years and older, urban residents, and ex-smokers, suggesting that these sub-groups should be priority populations of health screening and tobacco control related to TTFC.

Smoking is one of the important contributions for the chronic airway inflammation,26 which enhances excitability of vagal bronchopulmonary sensory nerves and increase tachykinin synthesis, causing the airway hyper-responsiveness and consequent respiratory disease.27 People breathe slowly and smoothly during sleep,28 on waking up, the breath volume and frequency increase immediately. In this case, morning cigarette smoking could heighten its toxic stimulation on respiratory system. For example, asthma is worse in the morning as compared to the evening.29 Nicotine dependence could be another plausible mechanism. A population-based study has shown that the highly dependent smokers inhale cigarette smoke more deeply and retain it in airways longer.30 Thus a higher dose of harmful cigarette smoke components enter body and a longer toxicity exposure aggravates the inflammation of respiratory system.

In contrast to American11 and European10 studies, we found no significant difference in associations between shorter (≤30 minutes) and longer (>30 minutes) TTFC with the prevalence of CRD among smokers in China. This disparity could be explained by the lower level of nicotine dependence in Chinese than that in other racial groups.32,33 First, TTFC is arguably the best single-item measure of nicotine dependence6 and, on average, Asians tend to have longer TTFC than the Europeans and Americans.32,34 which is partly evidenced in our study, showing that a larger proportion of TTFC with over 60 minutes in Chinese elderly compared with the European/American population (15.3% vs 13.2%). Second, nicotine dependence and smoking consumption are maintained by the pharmacologic effect of nicotine. Among Asians, a lower enzymatic activity of the CYP2A6*4 was detected,35 which can slow down the metabolism of the nicotine and cotinine (the primary proximate metabolite of nicotine).36,37 In addition, a study examining the nicotine toxicity following patch placement also found that the probability of nicotine-induced toxicity tended to be lower among Asians comparing with white people.38 Based on this evidence, we hypothesized that due to the relatively lower nicotine dependence and slower nicotine toxicity accumulation, the detrimental impact of tobacco on the respiratory system of the elderly Chinese smokers could be delayed to some extent. As the different distribution of TTFC among different ethnic groups, the threshold
Table 1. The univariate analysis of the prevalence of chronic respiratory diseases among people with different demographic characteristics ($n = 13,208$)

| Variables                                              | N (%)   | Unsuffered (%) | Suffered (%) | $\chi^2$ | $P$    |
|--------------------------------------------------------|---------|----------------|--------------|----------|--------|
| Sex                                                    |         |                |              |          |        |
| Male                                                   | 5,752 (43.5) | 4,944 (86.0) | 808 (14.0)  | 76.96    | <0.001 |
| Female                                                 | 7,456 (56.5) | 6,772 (90.8)  | 684 (9.2)    |          |        |
| Age, years                                             |         |                |              |          |        |
| 52–79                                                  | 4,597 (34.8) | 4,165 (90.6)  | 432 (9.4)    | 40.20    | <0.001 |
| 80–89                                                  | 3,330 (25.2) | 2,865 (86.0)  | 465 (14.0)   |          |        |
| ≥90                                                    | 5,281 (40.0) | 4,686 (88.7)  | 593 (11.3)   |          |        |
| Ruralitya                                              |         |                |              |          |        |
| Urban residents                                        | 3,607 (27.4) | 3,099 (85.9)  | 508 (14.1)   | 40.43    | <0.001 |
| Rural residents                                        | 9,548 (72.6) | 8,578 (89.8)  | 970 (10.2)   |          |        |
| Years of schooling                                     |         |                |              |          |        |
| No schooling                                           | 5,564 (42.1) | 4,976 (89.4)  | 588 (10.6)   | 5.09     | 0.078  |
| 1–6 years of schooling                                 | 4,883 (37.0) | 4,305 (88.2)  | 578 (11.8)   |          |        |
| ≥7 years of schooling                                  | 2,761 (20.9) | 2,435 (88.2)  | 326 (11.8)   |          |        |
| Marital statusb                                        |         |                |              |          |        |
| Married and live together                              | 5,187 (39.6) | 4,586 (88.4)  | 601 (11.6)   | 0.88     | 0.349  |
| Never married/separated/divorced/widowed               | 7,895 (60.4) | 7,022 (88.9)  | 873 (11.1)   |          |        |
| BMI, kg/m²                                             |         |                |              |          |        |
| Underweight (<18.5)                                   | 6,804 (51.5) | 6,030 (88.6)  | 774 (11.4)   | 2.93     | 0.232  |
| Normal (18.5–23.9)                                     | 2,262 (17.1) | 1,988 (87.9)  | 274 (12.1)   |          |        |
| Overweight/Obese (≥24)                                 | 4,142 (31.4) | 3,698 (89.3)  | 444 (10.7)   |          |        |
| Physical exercisec                                     |         |                |              |          |        |
| Yes                                                    | 3,917 (30.0) | 3,506 (89.5)  | 411 (10.5)   | 3.36     | 0.067  |
| No physical exercise                                   | 9,129 (70.0) | 8,070 (88.4)  | 1,059 (11.6) |          |        |
| Alcohol consumptiond                                   |         |                |              |          |        |
| Yes                                                    | 1,874 (14.4) | 1,692 (90.3)  | 182 (9.7)    | 5.60     | 0.018  |
| No                                                     | 11,162 (85.6) | 9,869 (88.4)  | 1,293 (11.6) |          |        |
| Sleep time                                             |         |                |              |          |        |
| <7 hours                                               | 4,753 (36.0) | 4,145 (87.2)  | 608 (12.8)   | 18.35    | <0.001 |
| 7–9 hours                                              | 5,551 (42.0) | 4,989 (89.9)  | 562 (10.1)   |          |        |
| ≥10 hours                                              | 2,904 (22.0) | 2,582 (88.9)  | 322 (11.1)   |          |        |
| Physical examinatione                                  |         |                |              |          |        |
| Regular physical examination                           | 8,910 (67.8) | 7,912 (88.8)  | 998 (11.2)   | 0.27     | 0.601  |
| No physical examination                                | 4,240 (32.2) | 3,752 (88.5)  | 488 (11.5)   |          |        |
| Fuel for cookingf                                      |         |                |              |          |        |
| No cooking                                             | 225 (1.8) | 199 (88.4)    | 26 (11.6)    | 7.41     | 0.025  |
| Electricity/Gas                                        | 8,654 (68.1) | 7,638 (88.3)  | 1,016 (11.7) |          |        |
| Coal/Firewood/Straw                                    | 3,822 (30.1) | 3,437 (89.9)  | 385 (10.1)   |          |        |
| Ventilation of the kitchen                             |         |                |              |          |        |
| No ventilation                                         | 1,140 (9.0) | 1,027 (90.1)  | 113 (9.9)    | 9.68     | 0.021  |
| Lampblack exhauster                                    | 4,364 (34.6) | 3,826 (87.7)  | 538 (12.3)   |          |        |
| Ventilation hood                                       | 950 (7.5) | 844 (88.8)    | 106 (11.2)   |          |        |
| Nature windowing ventilation                           | 6,166 (48.9) | 5,512 (89.4)  | 654 (10.6)   |          |        |
| Air cleaning in household                             |         |                |              |          |        |
| Yes                                                    | 1,042 (8.0) | 910 (87.3)    | 132 (12.7)   | 2.42     | 0.12   |
| No                                                     | 11,956 (92.0) | 10,631 (88.9) | 1,325 (11.1) |          |        |
| Distance to the arterial road                           |         |                |              |          |        |
| <100 m                                                 | 4,081 (31.3) | 3,563 (87.3)  | 518 (12.7)   | 14.81    | 0.002  |
| 101–300 m                                              | 2,350 (18.1) | 2,083 (88.6)  | 267 (11.4)   |          |        |
| >300 m                                                 | 5,732 (44.0) | 5,138 (89.6)  | 594 (10.4)   |          |        |
| Not sure                                               | 855 (6.6) | 771 (90.2)    | 84 (9.8)     |          |        |
| Distance to the nearest hospitalg                      |         |                |              |          |        |
| <1 km                                                  | 1,358 (10.4) | 1,170 (86.2)  | 188 (13.8)   | 11.47    | 0.009  |
| 1.0–2.9 km                                             | 8,094 (61.8) | 7,216 (89.2)  | 878 (10.8)   |          |        |
| 3.0–4.9 km                                             | 1,783 (13.6) | 1,591 (89.2)  | 192 (10.8)   |          |        |
| ≥5 km                                                  | 1,858 (14.2) | 1,638 (88.2)  | 220 (11.8)   |          |        |
| Daily smoking per day of persons living togetherh      |         |                |              |          |        |
| No cigarettes                                          | 6,374 (61.3) | 5,660 (88.8)  | 714 (11.2)   | 14.77    | 0.002  |
| 1–10 cigarettes                                        | 1,442 (13.9) | 1,282 (88.9)  | 160 (11.1)   |          |        |
| 11–20 cigarettes                                       | 1,455 (14.0) | 1,310 (90.0)  | 145 (10.0)   |          |        |
| >20 cigarettes                                         | 1,123 (10.8) | 959 (85.4)    | 164 (14.6)   |          |        |

Continued on next page.
for TTFC predicting the prevalence of CRD should be altered. A higher cut-off point of TTFC might be more suitable for exploring the relationship with the occurrence of CRD in older Chinese smokers.

Women appear to be more vulnerable to cigarette smoking and maintain a higher prevalence of respiratory disease. Throughout the human life span, female lungs tend to be smaller and to weigh less than male lungs, correspondingly, their airways are narrower in diameter than that of men. However, they exhibit higher forced expiratory flow rates, and the ratio of forced expiratory volume in one second to forced vital capacity ratios are higher in women. When smoking, women’s respiratory tracts are under more pressure, accelerating the toxic impact of tobacco composition on the tracheal cells. Except the difference in physiological structure, different nicotine metabolism between sexes could be another possible reason of the gender difference. Women generally metabolize nicotine more rapidly than men; thus, when consuming the same amount of nicotine, women may have higher exposure to harmful substances of cigarettes than men.

Table 2. Stepwise multivariate logistic regression analyses on the associations between TTFC and the prevalence of chronic respiratory diseases in seven models

| Models | Adjusted covariant | TTFC, minutes | N (%) | Unsuffered (%) | Suffered (%) | $\chi^2$ | P |
|--------|-------------------|---------------|-------|----------------|-------------|--------|----|
| Model 1 | None | No smoking | 9,429 (71.4) | 8,543 (90.6) | 886 (9.4) | 127.11 | <0.001 |
|        |       | <30 years | 682 (5.2) | 588 (86.2) | 94 (13.8) | 121.48 | <0.001 |
|        |       | 30–49 years | 1,203 (9.1) | 999 (83.0) | 204 (17.0) |        |    |
|        |       | 50–69 years | 1,403 (10.6) | 1,163 (82.9) | 240 (17.1) |        |    |
|        |       | ≥70 years | 491 (3.7) | 423 (86.2) | 68 (13.8) |        |    |
| Model 2 | Sex, Age | No smoking | 9,429 (71.4) | 8,543 (90.6) | 886 (9.4) | 121.48 | <0.001 |
|        |       | ≤30 minutes | 1,695 (12.8) | 1,407 (83.0) | 288 (17.0) |        |    |
|        |       | >30 minutes | 2,084 (15.8) | 1,766 (84.7) | 318 (15.3) |        |    |
| Model 3 | Sex, Age, Rurality, Years of schooling, Marital status, BMI | No smoking | 9,429 (71.5) | 8,543 (90.6) | 886 (9.4) | 170.12 | <0.001 |
|        |       | ≤30 minutes | 1,747 (13.2) | 1,397 (80.0) | 350 (20.0) |        |    |
|        |       | >30 minutes | 2,013 (15.3) | 1,762 (87.5) | 251 (12.5) |        |    |
| Model 4 | Sex, Age, Rurality, Alcohol consumption, Physical exercise, BMI, Sleep time, Years of schooling, Marital status | No smoking | 9,429 (71.4) | 8,543 (90.6) | 886 (9.4) | 126.46 | <0.001 |
|        |       | 1–10 cigarette | 2,027 (15.3) | 1,729 (85.3) | 298 (14.7) |        |    |
|        |       | >10 cigarette | 1,752 (13.3) | 1,444 (82.4) | 308 (17.6) |        |    |

BMI, body mass index; CI, confidence interval; OR, odds ratio; Ref., reference; TTFC, time to first morning cigarette after waking.

for TTFC predicting the prevalence of CRD should be altered. A higher cut-off point of TTFC might be more suitable for exploring the relationship with the occurrence of CRD in older Chinese smokers.

Women appear to be more vulnerable to cigarette smoking and maintain a higher prevalence of respiratory disease. Throughout the human life span, female lungs tend to be smaller and to weigh less than male lungs, correspondingly, their airways are narrower in diameter than that of men. However, they exhibit higher forced expiratory flow rates, and the ratio of forced expiratory volume in one second to forced vital capacity ratios are higher in women. When smoking, women’s respiratory tracts are under more pressure, accelerating the toxic impact of tobacco composition on the tracheal cells. Except the difference in physiological structure, different nicotine metabolism between sexes could be another possible reason of the gender difference. Women generally metabolize nicotine more rapidly than men; thus, when consuming the same amount of nicotine/cigarettes, women may have higher exposure to harmful substances of cigarettes than men.
Residents living in urban areas expose to more aerial pollution, which has been identified to be interacted with cigarette smoking, than those in rural areas, the combined effect is more detrimental to people’s respiratory health. In addition, the higher diagnosis rate of CRD among urban residents could partially attribute to their more convenient access to high-quality medical or healthcare services. In the past, false tobacco advertisement, poorer design (e.g., no filter tip), and adverse cigarette products (containing more tar, nicotine, or carbon monoxide) generated more harms to nowadays older population than those younger. Plus China’s traditional smoking beliefs and culture (cigarette gifting and sharing), the hazardous impact of smoking on the elderly smokers could be larger. Furthermore, our study also found that the shorter TTFC was more closely associated with the presence of chronic respiratory diseases than the longer TTFC in ex-smoker, while not in current smoker. There was nonetheless evidence of survivor bias in our study for the inevitable questions of the cross-section design. The current smokers in our analysis are generally healthier than those ex-smokers, as the latter might need to quit smoking because of smoke-related diseases. Moreover, a combination of survival bias, so-called healthy-smoker bias, and recall bias about the details of remote smoking history all could lead to these results.

This is the first national study on the association of the TTFC and the prevalence of CRD in Chinese elderly population. Most previous studies on this topic were conducted in other countries

Figure 2. Subgroup analyses on the relationship between the TTFC and the prevalence of CRD stratified by sex, age, rurality, past-present smoking status, and smoking amount per day. CI, confidence interval; CRD, chronic respiratory diseases; OR, odds ratio; Ref., reference; TTFC, time to first morning cigarette after waking.
or focused on younger adults. In fact, smoking control in
older people could bring significant gains in healthy life
expectancy and lower risks of disability. Therefore, this study
has clinical and public health implications, and the findings
provide a novel insight for smoking-related health education.
Further, participants in this study were from the nationwide
survey of CLHLS, which covers approximate 85% of China’s
citizens, so the findings have appropriate representativeness and
applicability.

Some limitations should be noted. First, this is only one round
of the CLHLS survey, the data of this study limited its ability to
identify the causal relationships between the TTFC and the
prevalence of CRD. Second, we adopt composite endpoints, the
CRD, in this study, which has made it difficult to assess the
impact of the TTFC on the risk of specific endpoint event. To
clarify the findings, further studies with separate respiratory
disease as outcome should be conducted. Third, smoking
exposure (from conventional cigarettes or from e-cigarettes and
heated tobacco products) was not specified in this study,
application of the findings to those who use e-cigarettes and
heated tobacco products should be careful. Fourth, some
comparative groups involved in the discussion were Asians or
Chinese origin population, rather than residents living in China, it
could limit the findings implication to some extent considering
disparities of lifestyle and environmental exposures.

In conclusion, the difference between shorter (≤30 minutes)
and longer (>30 minutes) TTFC on the prevalence of CRD was
statistically insignificant in Chinese elderly. However, the
shorter TTFC might increase the prevalence of CRD in females,
people aged 90 years and older, urban residents, and ex-smokers.
Our findings suggest that the use of TTFC as an indicator of the
prevalence of CRD in elderly Chinese smokers may not be as applicable as in the European and American populations,
but the underlying relationship of TTFC and the prevalence of
CRD among specific Chinese population warrants further research.

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opendata.pku.edu.cn/dataset.xhtml?persistentId=doi:10.18170/
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SUPPLEMENTARY MATERIAL

Supplementary data related to this article can be found at https://
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REFERENCES

1. Dwyer-Lindgren L, Bertozzi-Villa A, Stubbs RW, et al. Trends and
patterns of differences in chronic respiratory disease mortality
among US counties, 1980–2014. JAMA. 2017;318(12):1136–1149.
2. GBD Chronic Respiratory Disease Collaborators. Prevalence and
attributable health burden of chronic respiratory diseases, 1990–
2017: a systematic analysis for the Global Burden of Disease Study
2017. Lancet Respir Med. 2020;8(6):585–596.
3. Hartnett KP, Kite-Powell A, Patel MT, et al. Syndromic surveillance
for e-cigarette, or vaping, product use-associated lung injury. N Engl
J Med. 2020;382(8):766–772.
4. Xiao D, Chen Z, Wu S, et al. Prevalence and risk factors of small
airway dysfunction, and association with smoking, in China:
findings from a national cross-sectional study. Lancet Respir Med.
2020;8(11):1081–1093.
5. Yoshida K, Gowers KHC, Lee-Six H, et al. Tobacco smoking and
somatic mutations in human bronchial epithelium. Nature. 2020;
578(7794):266–272.
6. Selva AS, Oancea SC, Thapa S. Time to first cigarette, a proxy of
nicotine dependence, increases the risk of pulmonary impairment,
independently of current and lifetime smoking behavior. Nicotine
Tob Res. 2016;18(6):1431–1439.
7. Branstetter SA, Muscat JE, Mercincavage M. Time to first cigarette:
a potential clinical screening tool for nicotine dependence. J Addict
Med. 2020;14(5):409–414.
8. Hellberg U, Thacher J, Andersson N, et al. Smoking habits among
adolescents with asthma - data from a population-based birth cohort.
Allergy. 2019;74(5):1003–1005.
9. Guertin KA, Gu F, Wacholder S, et al. Time to first morning
and risk of chronic obstructive pulmonary disease: smokers in the
PLCO Cancer Screening Trial. PLoS One. 2015;10(5):
e0125973.
10. Gu F, Wacholder S, Kovalchik S, et al. Time to smoke first morning
cigarette and lung cancer in a case-control study. J Natl Cancer Inst.
2014;106(6):dju118.
11. Mathur C, Erickson DJ, Stigler MH, Forster JL, Finnegan JR Jr.
Individual and neighborhood socioeconomic status effects on
adolescent smoking: a multilevel cohort-sequential latent growth
analysis. Am J Public Health. 2013;103(3):543–548.
12. Chang Y, Kang HY, Lim D, Cho HJ, Khang YH. Long-term trends
in smoking prevalence and its socioeconomic inequalities in Korea,
1992–2016. Int J Equity Health. 2019;18(1):148.
13. Goodwin RD, Wall MM, Gbedemah M, et al. Trends in cigarette
consumption and time to first cigarette on awakening from 2002 to
2015 in the USA: new insights into the ongoing tobacco epidemic.
Tob Control. 2018;27(4):379–384.
14. Lugo A, La Vecchia C, Boccia S, Murisic B, Gallus S. Patterns of
smoking prevalence among the elderly in Europe. Int J Environ Res
Public Health. 2013;10(9):4418–4431.
15. Lim KH, Jasvindar K, Cheong SM, et al. Prevalence of smoking
and its associated factors with smoking among elderly smokers in
Malaysia: findings from a nationwide population-based study. Tob
Induc Dis. 2016;14:8.
16. He X, Song M, Qu J, et al. Major Program Expert Group. Basic and
translational aging research in China: present and future. Protein
Cell. 2019;10(7):476–484.
17. Vaz Fragoso CA, Lee PJ. The aging lung. J Gerontol A Biol Sci Med
Sci. 2012;67(3):233–235.
18. Wang C, Xu J, Yang L, et al. Prevalence and risk factors of chronic
obstructive pulmonary disease in China (the China Pulmonary
Health [CPH] study): a national cross-sectional study. Lancet. 2018;
391(10131):1706–1717.
19. Zeng Y, Feng Q, Hesketh T, Christensen K, Vaupel JW. Survival,
disabilities in activities of daily living, and physical and cognitive
functioning among the oldest-old in China: a cohort study. Lancet.
2017;389(10079):1619–1629.
20. Lv YB, Gao X, Yin ZX, et al. Revisiting the association of blood
pressure with mortality in oldest old people in China: community
based, longitudinal prospective study. BMJ. 2018;361:k2158.
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21. Lv X, Li W, Ma Y, et al. Cognitive decline and mortality among community-dwelling Chinese older people. *BMJ Med. 2019;17(1):63.*

22. Weisell RC. Body mass index as an indicator of obesity. *Asia Pac J Clin Nutr. 2002;11(s8):S681–S684.*

23. Rubin D. *Multiple Imputation for Nonresponse in Surveys.* New York; 1987.

24. Altman DG, Bland JM. Interaction revisited: the difference between two estimates. *BMJ. 2003;326(7382):219.*

25. Nye RT, Mercincavage M, Branstetter SA. Time to first cigarette, physical activity, and pulmonary function in middle-aged to older adult smokers. *J Phys Act Health. 2017;14(8):612–616.*

26. Kou YR, Kwong K, Lee LY. Airway inflammation and hypersensitivity induced by chronic smoking. *Respir Physiol Neurobiol. 2011;178(3):395–405.*

27. Guo M, Liu Y, Han X, et al. Tobacco smoking aggravates airway inflammation by upregulating endothelin-2 and activating the c-Jun amino terminal kinase pathway in asthma. *Int Immunopharmacol. 2019;77:105916.*

28. Goyal M, Goel A, Singh R, et al. Circadian rhythm of airways caliber and its autonomic modulation. *Chronobiol Int. 2020;37(6):845–855.*

29. Campana LM, Malhotra A, Suki B, et al. The effect of lung stretch during sleep on airway mechanics in overweight and obese asthma. *Respir Physiol Neurobiol. 2013;185(2):304–312.*

30. Jiménez-Ruiz CA, Masa F, Miravitlles M, et al. Smoking characteristics: differences in attitudes and dependence between healthy smokers and smokers with COPD. *Chest. 2001;119(5):1365–1370.*

31. Schnoll RA, Goren A, Annunziata K, Suaya J. The prevalence, predictors and associated health outcomes of high nicotine dependence using three measures among US smokers. *Addiction. 2013;108(11):1989–2000.*

32. Branstetter SA, Mercincavage M, Muscat JE. Predictors of the nicotine dependence behavior time to the first cigarette in a multi-racial cohort. *Nicotine Tob Res. 2015;17(7):819–824.*

33. Herzog TA, Pokhrel P. Ethnic differences in smoking rate, nicotine dependence, and cessation-related variables among adult smokers in Hawaii. *J Community Health. 2012;37(6):1226–1233.*

34. Kim SS, Ziedonis D, Chen KW. Tobacco use and dependence in Asian Americans: a review of the literature. *Nicotine Tob Res. 2007;9(2):169–184.*

35. Ozaki S, Oyama T, Isse T, et al. Smoking cessation program and CYP2A6 polymorphism. *Front Biosci. 2006;11:2590–2597.*

36. Oscarson M, McLellan RA, Gullstén H, et al. Characterisation and PCR-based detection of a CYP2A6 gene deletion found at a high frequency in a Chinese population. *FEBS Lett. 1999;448(1):105–110.*

37. Nakajima M, Yamamoto T, Nunoya K, et al. Characterization of CYP2A6 involved in 3′-hydroxylation of cotinine in human liver microsomes. *J Pharmocol Exp Ther. 1996;277(2):1010–1015.*

38. Dempsey DA, Sti Helen G, Jacob P 3rd, Tyndale RF, Benowitz NL. Genetic and pharmacokinetic determinants of response to transdermal nicotine in white, black, and Asian nonsmokers. *Clin Pharmacol Ther. 2013;94(6):687–694.*

39. Erbas B, Knudsen TM, Janson C, et al. Critical age windows in the impact of lifetime smoking exposure on respiratory symptoms and disease among ever smokers. *Environ Res. 2018;164:241–247.*

40. Troisi RJ, Speizer FE, Willett WC, Trichopoulos D, Rosner B. Menopause, postmenopausal estrogen preparations, and the risk of adult-onset asthma. A prospective cohort study. *Am J Respir Crit Care Med. 1995;152(4 Pt 1):1183–1188.*

41. Martin SE, Mathur R, Marshall I, Douglas NJ. The effect of age, sex, obesity and posture on upper airway size. *Ear Res J. 1997;10(9):2087–2090.*

42. Becklake MR, Kauffmann F. Gender differences in airflow behaviour over the human life span. *Thorax. 1999;54(12):1119–1138.*

43. Piper ME, Cook JW, Schlam TR, et al. Gender, race, and education differences in abstinence rates among participants in two randomized smoking cessation trials. *Nicotine Tob Res. 2010;12(6):647–657.*

44. Benowitz NL, Swan GE, Jacob P 3rd, Lessov-Schlaggar CN, Tyndale RF. CYP2A6 genotype and the metabolism and disposition kinetics of nicotine. *Clin Pharmacol Ther. 2006;80(5):457–467.*

45. Lin H, Guo Y, Koval P, et al. Exposure to air pollution and tobacco smoking and their combined effects on depression in six low- and middle-income countries. *Br J Psychiatry. 2017;211(3):157–162.*

46. Harris B. The intractable cigarette ‘filter problem’. * Tob Control. 2011;20(Suppl 1):i10–116.*

47. McDaniel PA, Malone RE. "I always thought they were all pure tobacco": American smokers’ perceptions of “natural” cigarettes and tobacco industry advertising strategies. *Tob Control. 2007;16(4):258–263.*

48. Jaine R, Healey B, Edwards R, Hoek J. How adolescents view the tobacco endgame and tobacco control measures: trends and associations in support among 14–15 year olds. *Tob Control. 2015;24(5):449–454.*

49. Hodder RK, Freund M, Wolfenden L, et al. Systematic review of universal school-based ‘resilience’ interventions targeting adolescent tobacco, alcohol or illicit substance use: a meta-analysis. *Prev Med. 2017;100:248–268.*

50. Tian X, Tang Z, Jiang J, et al. Effects of smoking and smoking cessation on life expectancy in an elderly population in Beijing, China, 1992–2000: an 8-year follow-up study. *J Epidemiol. 2011;21(5):376–384.*

51. Gasperini B, Barbadoro P, Cherubini A, et al. The earlier the better: health-related quality of life is inversely related to age of smoking cessation in older former Italian smokers. *Aging Clin Exp Res. 2017;29(4):655–663.*