

# Association of smoking with poor health-related quality of life among health-profession students in China: A 31-university multilevel, multivariable analysis

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## ABSTRACT

**INTRODUCTION** While many studies have confirmed that smoking is causally associated with various diseases, some have found an association between smoking and human functional impairment. Relationships between smoking and poor health-related quality of life (HRQoL) have been investigated in general populations. However, these studies have examined only individual-level correlates. This study examined the association between smoking and poor HRQoL, at both the individual and contextual levels, in university settings across China.

**METHODS** Large-scale survey sampling was conducted among 11659 health-profession students from 31 Chinese universities. HRQoL was measured by the EQ-5D instrument. This multilevel, multivariable analysis utilized unadjusted and adjusted methods.

**RESULTS** Prevalence of poor HRQoL in this study was 2.7% (95% CI: 1.9–3.5). Multilevel logistic regression analysis revealed that frequent (OR=3.18; 95% CI: 2.35–4.33) and occasional smokers (OR=2.73; 95% CI: 1.61–4.65) and universities with high (OR=2.68; 95% CI: 1.34–5.35) and medium smoking prevalence (OR=1.49; 95% CI: 0.95–5.35) had excess odds of poor HRQoL compared to their respective referents, non-smokers and universities with a low smoking prevalence.

**CONCLUSIONS** This multilevel study provides new evidence that smoking is associated with poor HRQL. Findings underscore the importance of alerting the populace that functional impairment is linked to smoking.

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## INTRODUCTION

Smoking is considered the single most important avoidable cause of mortality in the world. Many studies have confirmed that smoking is causally associated with various diseases and conditions, including pulmonary diseases, cardiovascular diseases, cancer and mental disorders<sup>1</sup>. Tobacco kills more than 8 million people annually across the globe<sup>2</sup>. More than 7 million of these deaths are the result of direct tobacco use, while approximately 1.2 million emanate from non-smokers being exposed to secondhand smoke<sup>2</sup>. In China, approximately 1 million deaths annually are attributable to tobacco smoking, which includes 100000 deaths among non-smokers exposed to secondhand smoke (SHS)<sup>3</sup>. Some studies have found an association between smoking and human functional impairment<sup>2</sup>. Exploring the association between smoking and human functioning would provide

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additional evidence that smoking is harmful to health, but more importantly, help to elucidate the smoking risk mechanism<sup>2</sup>.

According to the Stimulus, Stress Response and Health (SRH) problems model, various stimuli (S) induce stress responses (R), which in turn, may induce disease<sup>4</sup>. Poor health-related quality of life (HRQoL) may occur due to mental stress that is rooted in behavioral problems<sup>2</sup>. This means that smoking is a strong stimulus that plausibly induces people to experience high mental stress, which in turn promotes poor HRQoL. There is a growing body of evidence suggesting that smoking is associated with increases in high levels of perceived stress<sup>5,6</sup>. The causal direction of the relationship is mixed. The psychological and biological theory argues that stress may increase hypothalamus-pituitary-adrenal (HPA) axis reactivity, negative emotions, physiologic reactivity, and therefore craving for nicotine<sup>7,8</sup>. However, many studies, especially intervention studies, have found that smoking may induce mental stress<sup>9,10</sup>. In addition, some studies have found that the increased level of exposure to SHS is positively associated with stress<sup>11-14</sup>. These findings imply that smoking has an effect on mental stress. In turn, mental stress is likely associated with a poor quality of life. The notion that a person's appraisal of his or her own stress will impact their physical and mental health (HRQoL) derives from the Transactional Model of Stress and Coping<sup>14,15</sup>. Many studies have found that mental stress may induce poor HRQoL<sup>15,16</sup>.

HRQoL is a comprehensive measure of physical, social and mental functioning, that has been used to estimate the impact of chronic disease, identify health disparities in populations, and to inform policies and patient management<sup>17</sup>. Relationships between smoking and HRQoL have been investigated in general populations<sup>18-23</sup>. However, most of these studies were conducted in high-income countries<sup>18-22</sup>, and only a few in middle- and low-income countries<sup>23,24</sup>.

Ecological models have emphasized that HRQoL is influenced by both individual and environmental variables<sup>4</sup>. However, these studies have examined only individual-level correlates, and no attention has been paid to the relative impact of both individual-level and contextual variables upon HRQoL. Variation in residential environments is plausibly a product of heterogeneity in social, mental, and behavioral factors,

as well as in socioeconomic development. There are two flaws in prior studies, which were all limited to individual-level data. On the one hand, those studies did not adjust for the relative impact of contextual confounders upon the association between smoking and HRQoL; consequently, their results may be biased. On the other hand, not combining individual with contextual-level data may fuel ecologic and atomistic fallacies, with the need to distinguish individual-level and contextual correlates of HRQoL<sup>25</sup>. The Chinese mainland occupies vast territory, with a diverse culture and great heterogeneity in economic and social development. By utilizing a large-scale, national population sample, this study was able to obtain information on the impact of both environmental and individual-level factors on poor HRQoL. Moreover, contextual variables have been shown to be stable representatives of environmental influences. Thus, this multilevel study of the association between smoking in universities and poor HRQoL could generate more reliable results than studies confined to individual-level data.

## METHODS

### Study design and sampling procedure

This study employed data from a 'tobacco control advocacy capacity building' project that was conducted in medical universities across China<sup>26</sup>. A series of related projects covered all provinces in China and included 103 universities located in 81 different cities<sup>27</sup>. The data for this study originated in a baseline survey on smoking beliefs, attitudes and behaviors of university students in the fourth project entitled 'Building tobacco treatment capacity in medical universities and affiliated hospitals in China'. Participants were health-profession students, which comprised medical, nursing and other students in health-related programs. The sampling procedure used an observational cross-sectional, multilevel approach with a multi-stage cluster sampling design. In Stage 1, this project included 50 universities – about 60% (31 universities) of them were involved in the baseline survey – that were selected from across China and differentiated by regional location. Selection of universities and colleges utilized probability proportional to size sampling applied to six different regions: the northeast, north, northwest, southwest, and east<sup>28</sup>. Of the selected universities, 18

were medical universities offering mainly medical, nursing and other health-related programs, and 13 were comprehensive universities offering both medical and non-medical programs. In total, 31 participating universities and colleges are located across China, extending from Harbin in the north to Guangdong in the south, to Xinjiang and Xizang in the west and Hangzhou in the east. The geographical distribution of the sample of institutions aligns with the total distribution.

In Stage 2, the sampling strategy involved the selection of levels within each university. All levels that had medical/health courses were included. In Stage 3, one-third of the courses were randomly selected from each level. On average, two classes were selected to participate in the study at each university. In Stage 4, all students in these selected classes were surveyed.

### Data collection

Individual variables were measured via a structured self-administered questionnaire. This questionnaire was administered during regular classes and took approximately 30 minutes to complete. All responses were anonymous. A common research protocol was used across all 31 universities to assure homogeneity of questionnaire administration and data collection procedures. The study was approved by the Ethics Committee at the Zhejiang University Medical Center, and verbal consent was obtained from all participants before data collection.

### Measures

#### *Dependent variable: HRQoL*

In this study, HRQoL was measured using the EQ-5D instrument, which describes health in five dimensions<sup>29</sup>. It is simple to operate and be comprehended by the subjects and manifests good reliability and validity. EQ-5D is increasingly being used to assess public health issues and is now a common instrument in population-based survey research on HRQoL<sup>30-32</sup>. The Chinese version of the EQ-5D has been used in mainland China<sup>33-35</sup>. However, its reliability and validity were unreported in most studies except that of Wang et al.<sup>36</sup>. The study determined that the Chinese EQ-5D showed fair to moderate levels of test-retest reliability. The scores had moderate or strong correlations with all SF-36 scores. However, their study did not report

the results of the test for internal reliability. In our study, the Cronbach alpha coefficient of the EQ-5D is 0.56, which approaches the lowest value (0.6) requirements for consistency<sup>4</sup>. In concert with the Wang et al.<sup>36</sup> study results, we deem that the Chinese EQ-5D has acceptable reliability and validity. It taps mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each question allowed for three alternative responses: ‘no problems’, ‘some or moderate problems’, and ‘extreme problems’. They were coded 1, 2 and 3 and cumulated to form a total score for HRQoL<sup>23</sup>.

Departing from prior practice, where assessment scores of HRQoL were measured as a continuous variable<sup>18-23</sup>, HRQoL was dichotomized as normal and poor in our study. We employed HRQoL as a categorical variable because the quantitative comparisons produced highly sensitive differences in statistical difference tests in a large sample, and often the results obtained from a large sample statistical test could not be replicated in a small sample statistical test<sup>4</sup>. Furthermore, if the variable was represented numerically, HRQoL level related to assessment scores cannot clearly distinguish higher from lower. It is important to consider the characteristics of the variable instead of automatically assuming it is numeric. Finally, in considering professional significance, it is more comprehensible to stakeholders if HRQoL results are presented as normal or poor – similar to normal or high blood pressure and mental stress readings. For this analysis, responses to EQ-5D of at least two ‘moderates’ or one ‘extreme’ were classified as poor quality of life<sup>4</sup>.

Information regarding smoking status was assessed using standard methods. For the behavioral smoking measure, we employed the method recommended by the World Health Organization<sup>37</sup>, as utilized in the Global Adult Tobacco Survey (GATS). We defined a current smoker as someone who smoked cigarettes at the time of interview, a daily smoker as someone who smoked every day, and an occasional smoker as someone who smoked on some days<sup>1,37</sup>. The independent variable was smoking status and coded as: 1=non-smoker, 2=occasional smoker, and 3=daily smoker. University-level current smoking status was based on an aggregation of individual-level current smoking responses, with current smoking prevalence distinguished as: <5%, 5–9.9%, and ≥10% (Table 1).

**Table 1. Characteristics of the study sample and poor health-related quality of life prevalence among health-profession students from 31 Chinese universities (N=11659)**

Characteristics	n	Percent of sample	Percent prevalence	OR (95% CI)
<b>Individual level</b>				
<b>Age (years)</b>				
<19 (Ref.)	2355	20.2	1.7	1
19–19.9	2367	20.3	3.0	1.83 (1.32–2.53)**
20–20.9	2623	22.5	2.5	1.48 (1.01–2.18)*
21–21.9	2192	18.8	3.2	1.94 (1.21–3.13)**
≥22	2122	18.2	3.2	1.90 (1.22–2.98)**
<b>Sex</b>				
Male (Ref.)	3722	33.2	3.7	1
Female	7937	66.8	2.2	0.60 (0.48–0.75)**
<b>Ethnicity</b>				
Han (Ref.)	10713	86.0	2.4	1
Minority	946	14.0	4.7	2.03 (1.46–2.83)**
<b>Father's education level</b>				
Elementary school or lower (Ref.)	1980	35.0	3.6	1
Junior high school	4511	36.6	2.2	0.59 (0.33–1.07)
High school	2741	20.8	2.8	0.77 (0.56–1.06)
Junior college	1294	11.3	2.1	0.58 (0.37–0.90)*
College	1133	6.2	3.0	0.84 (0.54–1.31)
<b>Mother's education level</b>				
Elementary school or lower (Ref.)	3201	33.1	3.0	1
Junior high school	4347	34.4	2.6	0.86 (0.63–1.18)
High school	2250	16.9	2.3	0.76 (0.47–1.23)
Junior college	1114	9.7	1.8	0.59 (0.30–1.19)
College	747	5.9	12.6	1.28 (0.87–1.92)
<b>Father's occupation</b>				
Managerial (Ref.)	890	7.2	3.1	1
Professional	767	6.7	4.3	1.40 (0.96–2.03)
Business and services	1913	14.6	2.9	0.93 (0.38–2.27)
Technical	1785	15.0	2.2	0.68 (0.36–1.29)
Operational	3359	29.4	2.1	0.67 (0.36–1.26)
Retired	150	1.4	7.0	2.31 (0.94–5.68)
Not employed	515	5.0	3.9	1.24 (0.71–2.18)
Other	2280	20.7	2.4	0.76 (0.41–1.42)
<b>Mother's occupation</b>				
Managerial (Ref.)	511	4.6	6.2	1
Professional	782	6.6	4.4	0.70 (0.39–1.26)
Business and services	2017	15.8	2.7	0.43 (0.20–0.91)*
Technical	823	6.8	1.7	0.26 (0.10–0.66)**

Continued

Table 1. Continued

Characteristics	n	Percent of sample	Percent prevalence	OR (95% CI)
Operational	2781	24.5	2.1	0.32 (0.15–0.70)**
Retired	290	2.2	6.6	1.08 (0.51–2.28)
Unemployed	2181	18.8	2.6	0.40 (0.19–0.86)**
Other	2274	20.5	2.1	0.33 (0.16–1.65)**
<b>Major</b>				
Public health (Ref.)	2589	24.6	3.0	1
Clinical	6402	59.6	2.5	0.85 (0.60–1.20)
Nurse	1067	6.5	2.6	0.86 (0.45–1.64)
Other	1601	9.2	2.5	0.84 (0.53–1.32)
<b>Academic achievement in class</b>				
Top third (Ref.)	3902	33.9	2.4	1
Middle third	5426	48.6	2.6	1.04 (0.80–1.35)
Bottom third	2331	20.5	3.3	1.34 (0.83–2.17)
<b>Monthly expenses (RMB)</b>				
<1000 (Ref.)	3998	33.6	2.5	1
1000–1499	5364	41.5	2.6	1.01 (0.76–1.34)
≥1500	2297	21.9	3.2	1.25 (0.81–1.94)
<b>Smoking status</b>				
Non-smoker (Ref.)	10847	92.2	2.0	1
Occasional smoker	458	4.3	9.4	5.18 (3.29–8.18)**
Daily smoker	354	3.5	13.6	7.88 (5.33–11.65)**
<b>Alcohol status</b>				
Non-drinker (Ref.)	8322	69.7	1.7	1
Occasional drinker	3194	29.0	4.1	2.56 (2.10–3.13)**
Daily drinker	143	1.3	26.2	21.21 (9.99–45.01)**
<b>University-level smoking prevalence (%)</b>				
<5 (Ref.)	3855	17.9	1.4	1
5–9	7183	75.2	2.0	1.40 (0.91–2.14)
≥10	621	6.9	4.1	2.93 (1.70–5.06)**
<b>Contextual level</b>				
<b>Home location</b>				
Countryside or township (Ref.)	7079	62.8	2.7	1
County town	2002	15.8	3.1	1.16 (0.85–1.58)
City	2578	21.4	2.3	0.86 (0.62–1.18)
<b>University ranking</b>				
Low (Ref.)	3276	17.0	2.7	1
Medium	7481	68.1	1.8	0.66 (0.41–1.06)
High	902	14.8	2.6	0.96 (0.42–2.22)

Continued

Table 1. Continued

Characteristics	n	Percent of sample	Percent prevalence	OR (95% CI)
<b>City per capita GDP (RMB)</b>				
<8000 (Ref.)	6084	58.6	1.8	1
8000–11999	3445	25.7	2.6	1.45 (0.75–2.79)
≥12000	2130	15.7	1.8	0.98 (0.50–1.90)
<b>Population (in ten thousands)</b>				
<200 (Ref.)	6574	55.6	1.9	1
200–499	3067	32.1	2.1	0.66 (0.41–1.06)
≥500	2018	12.3	2.6	0.96 (0.42–2.22)
<b>City population density (persons/km<sup>2</sup>)</b>				
<800 (Ref.)	6359	58.6	6.6	1
800–1199	2762	23.1	4.0	0.59 (0.37–0.94)*
≥1200	2538	18.4	2.7	0.38 (0.21–0.72)**

### Individual-level control variables

Many studies have found that individual-level demographic and socioeconomic variables may influence HRQoL<sup>38–40</sup>. In this study, sociodemographic characteristics included age, sex, ethnicity, paternal and maternal occupation, academic major and achievement, and monthly expenses. Academic achievement was measured by asking respondents their class position: upper third (high), middle third (medium), or lower third (low). Monthly expenses were derived from the question: ‘How much do you spend each month?’.

#### Alcohol use

Smoking and alcohol use often co-occur, and both smoking and excessive alcohol consumption are harmful to health<sup>4</sup>. Alcohol use was ascertained by the question: ‘Do you drink alcohol?’; options were ‘no’, ‘drink alcohol on some days’ (occasionally), and ‘drink alcohol every day’ (daily). Responses were coded as: 1=non-drinker, 2=occasional drinker, and 3=daily drinker.

### Contextual control variables

HRQoL may be influenced by the environment<sup>4</sup>.

#### Home and university environment control variables

Some studies show that family environment is associated with HRQoL<sup>30,31</sup>. We included a measure

of the location of the home because this can reflect the socioeconomic position of the family, and social and economic development varies greatly between rural and urban areas<sup>4</sup>. Family location of students was differentiated as: countryside, township, county town, or city.

Heterogeneity in social resources and academic prestige of universities may influence student HRQoL<sup>4,39</sup>. University type was determined using the China university ranking system (low, middle, and high) implemented by the National Ministry of Education<sup>41</sup>.

#### City-level environment control variables

The first environmental contextual variable included in this study was the economic level of the cities in which the students were studying, measured by per capita Gross Domestic Product (GDP) in RMB (1000 Chinese Renminbi about US\$140). Since larger city size is frequently accompanied by increased stress and poor HRQoL, this population variable was also included. Also frequently, population density is positively associated with scarce resources, environmental pollution, traffic congestion, and other urban problems, and hence also is often accompanied by increased stress. This variable was included as a contextual variable because it may lead to poor HRQoL. The source was the National Bureau of Statistics<sup>28</sup>. The preceding categorizations were based

on prior practice<sup>42</sup>. Moreover, our sensitivity analyses using different categorizations of these variables produced similar results.

### Data analysis

All data were entered into a database using Microsoft Excel; data quality was ensured by double data entry. The dataset was imported into SAS (9.4 version) for statistical analyses. Descriptive statistics were calculated for poor HRQoL prevalence, together with 95% confidence intervals, across smoking use and individual and contextual control variables. Both unadjusted and adjusted analyses were conducted in assessing the association between smoking and poor HRQoL. SAS survey logistic procedures were applied in the unadjusted analysis, using the university as the clustering unit, in order to account for within-clustering correlation attributable to the complex sample. Associations were confirmed through the application of a multilevel logistic regression model, using the SAS GLIMMIX procedure<sup>43</sup>.

We built several multilevel models for this analysis. We estimated both fixed and random effects; the former explains the variation of HRQoL at the individual level and the latter at the contextual level<sup>43</sup>. We commenced with the Null Model, a three-level (individual, university, and university city) model with random intercepts, which did not include any predictors except a constant, in assessing variation in individuals experiencing poor HRQoL. From this base, we constructed four additional models. They were: the individual characteristics model (Model 1); individual-level model (Model 2), which adjusted demographic variables and alcohol status; university-level model (Model 3), which examined both individual and university level smoking status and poor HRQoL – the covariates adjusted in this model are the same as for Model 2; and the city-level model (Model 4), which is based on Model 3 with an added adjusted environmental covariate, population density; and the last model was conceived to examine any change in the association between smoking and poor HRQoL after alcohol status was excluded (Model 5). Model fitting was assessed by the likelihood of a change in the  $-2$  log and significance of the parameter (fix and random) variance estimates by the t-test statistic<sup>43</sup>.

All analyses were weighted: sampling weights were the inverse of the probability of selection of the

university; post-stratification weights were calculated in relation to sex, based on the estimated distributions of this characteristic from a national survey<sup>44</sup>. Final overall weights were computed as the product of the prior two weights. We did not consider using a non-response weight because non-response rates were low in this study.

### RESULTS

A total of 11802 individuals were identified as potential subjects. After excluding incomplete responses, a final sample generated 11659 valid responses. Of respondents completing surveys, 20.2% were aged <20 years, 61.9% were aged 20–21.9 years, and the remainder were aged  $\geq 22$  years. The sex distribution was 33.2% male and 66.8% female. The large majority of respondents, 86.0%, were Han and 14.0% were a minority (Table 1).

The survey yielded 280 responses of poor HRQoL from 11659 respondents, a prevalence of 2.7% (95% CI: 1.9–3.5). The distribution of poor HRQoL prevalence across different sociodemographic groups is reported in Table 1. The unadjusted analysis showed that, compared to their respective referents, non-smokers and universities with a low prevalence of current smoking, frequent (OR=7.88; 95% CI: 5.33–11.65) and occasional smokers (OR=5.18; 95% CI: 3.29–8.18) and universities with high (OR=2.93; 95% CI: 1.70–5.06) and medium smoking prevalence (OR=1.40; 95% CI: 0.91–2.14) had excess odds of poor HRQoL. Adjusted all individual, university and city-confounding variables results revealed that frequent (OR=3.18; 95% CI: 2.35–4.33) and occasional smokers (OR=2.73; 95% CI: 1.61–4.65) and universities with high (OR=2.68; 95% CI: 1.34–5.35) and medium smoking prevalence (OR=1.49; 95% CI: 0.95–5.35) had excess odds of poor HRQoL compared to their respective referents, non-smokers and universities with a low smoking prevalence (Table 2). However, differences in the point estimated odds ratios for frequent versus occasional smokers and high versus medium smoking prevalence universities were not statistically significant, given overlapping 95% confidence intervals.

The adjusted analysis showed that both frequent and occasional drinkers of alcohol had higher odds than non-drinkers of poor HRQoL. Moreover, the point-estimated odds ratio for the association

**Table 2. Factors associated with poor HRQoL as assessed in multilevel multivariable analyses among health-profession students from 31 Chinese universities (N=11659)**

Group	Null model	Individual characteristics (Model 1)	Individual level (Model 2)	University level (Model 3)	City level (Model 4)	City level (Model 5)
<b>Age (years)</b>						
<19 (Ref.)		1	1	1	1	1
19–19.9		1.78 (1.34–2.38)**	1.67 (1.27–2.18)**	1.70 (1.23–2.36)**	1.65 (1.21–2.25)**	1.76 (1.29–2.39)**
20–20.9		1.38 (0.97–1.97)	1.38 (0.90–1.87)	1.22 (0.90–1.66)	1.19 (0.86–1.64)	1.34 (0.91–2.37)
21–21.9		1.79 (1.14–2.80)*	1.60 (1.04–2.49)*	1.60 (1.11–2.25)*	1.46 (1.03–2.07)*	1.68 (1.18–2.09)**
≥22		1.73 (1.21–2.46)**	1.45 (1.03–2.53)*	1.57 (1.12–2.76)*	1.33 (0.95–1.85)	1.52 (1.11–2.09)**
<b>Ethnicity</b>						
Han (Ref.)		1	1	1	1	1
Minority		1.89 (1.25–2.85)**	1.68 (1.11–2.53)**	1.95 (1.37–2.76)**	1.72 (1.20–2.31)**	1.69 (1.17–2.44)**
<b>Mother's occupation</b>						
Managerial (Ref.)		1	1	1	1	1
Professional		0.75 (0.40–1.43)	0.77 (0.39–1.52)	0.75 (0.35–1.63)	0.74 (0.34–1.63)	0.75 (0.40–1.42)
Business and services		0.46 (0.26–0.83)*	0.52 (0.28–0.95)*	0.48 (0.24–0.96)*	0.50 (0.25–1.00)	0.55 (0.25–1.18)
Technical		0.52 (0.27–0.98)*	0.58 (0.29–1.13)	0.57 (0.24–1.35)	0.58 (0.24–1.38)	0.29 (0.10–0.84)*
Operational		0.31 (0.17–0.57)**	0.34 (0.18–0.63)**	0.31 (0.16–0.61)**	0.33 (0.17–0.65)**	0.31 (0.11–0.92)*
Retired		0.77 (0.28–2.16)	0.79 (0.29–2.16)	0.80 (0.31–2.07)	0.76 (0.29–2.00)	0.78 (0.30–2.03)
Not employed		0.55 (0.34–0.91)*	0.61 (0.37–1.00)	0.57 (0.30–1.10)	0.58 (0.30–1.12)	0.45 (0.18–1.15)
Other		0.43 (0.27–0.71)**	0.46 (0.27–0.77)**	0.45 (0.23–0.87)*	0.46 (0.24–0.89)*	0.29 (0.12–0.73)**
<b>Smoking status</b>						
Non-smoker (Ref.)			1	1	1	1
Occasional smoker			2.86 (1.71–2.26)**	2.71 (1.61–4.58)**	2.73 (1.61–4.65)**	4.22 (2.34–7.62)**
Frequent smoker			3.39 (2.43–4.75)**	3.27 (2.42–4.42)**	3.18 (2.35–4.33)**	6.33 (3.99–9.85)**
<b>Alcohol status</b>						
Non-drinker (Ref.)			1	1	1	
Occasional drinker			1.85 (1.51–2.26)**	1.83 (1.51–2.22)**	1.81 (1.50–2.19)**	
Frequent drinker			7.83 (3.21–19.10)**	13.14 (6.25–28.31)**	7.04 (2.89–17.14)**	
<b>University-level smoking prevalence (%)</b>						
<5 (Ref.)				1	1	1
5–9				1.54 (1.09–2.15)*	1.49 (0.95–5.34)	1.55 (0.98–2.46)
≥10				2.52 (1.20–5.28)*	2.68 (1.34–5.35)**	2.94 (1.46–5.92)**
<b>Population density (persons/km<sup>2</sup>)</b>						
<800 (Ref.)					1	1
800–1199					0.63 (0.42–0.97)*	0.91 (0.47–1.76)*
≥1200					0.41 (0.25–0.79)**	0.54 (0.36–0.81)**
Fixed parameters	3.86**	3.14**	3.09**	2.68**	3.11**	3.05**
Random parameters between universities	1.43**	1.56**	1.44**	1.19**	1.24**	1.19**
Random parameters between cities	0.56**	0.51**	0.49**	0.41**	0.34**	0.37**

Model 1: individual characteristics model. Model 2: individual-level model which adjusted for demographic variables and alcohol status. Model 3: university-level model which examined both individual and university level smoking status and poor HRQoL; the covariates adjusted in this model are the same as for Model 2. Model 4: city-level model is based on Model 3 with an added adjusted environmental covariate, population density. Model 5: conceived to examine any change in the association between smoking and poor HRQoL after alcohol status was excluded.

between frequent (daily) drinkers and poor HRQoL (OR=7.04; 95% CI: 2.89–17.14) was significantly higher statistically than that for occasional drinkers (OR=1.81; 95% CI: 1.50–2.19). A sensitivity analysis, whereby alcohol status was eliminated from the full model (Model 4), showed a marked increase in the magnitude of the respective point-estimated odds ratios for frequent (OR=6.33; 95% CI: 3.99–9.85) and occasional smokers (OR=4.22; 95% CI: 2.34–7.62), but did not alter the nature of the basic associations of smoking status with low HRQoL.

## DISCUSSION

In this study, we sought to quantify the association between smoking and poor health-related quality of life (HRQoL). We found that the prevalence of poor HRQoL among health-profession university students in this representative nationwide sample was 2.7% (95% CI: 1.9–3.5). Smoking was associated with poor HRQoL. This association can be explained by the SRH model. Smoking is a strong stimulus that plausibly induces people to have high mental stress, which in turn promotes poor HRQoL<sup>1</sup>.

This study has a number of strengths. First, we found that not only at the individual level but also at the university level smoking was associated with poor HRQoL. By design, this multilevel, multivariable study generated more reliable results than those from many prior individual-level studies. Secondly, our results showed that both daily and occasional smoking were associated with poor HRQoL. Although the point-estimated odds ratio was higher for the former than the latter, two groups were not significantly different statistically from each other given overlapping 95% confidence intervals. This finding likely reflects the relative youth of the study subjects. Nonetheless, the observed difference in the respective point-estimated odds ratios is consistent with biological plausibility. There was a statistically significant difference in the respective point-estimated odds ratios for the associations between daily and occasional drinking of alcohol and poor HRQoL, indicating an added hazard for being a regular drinker at younger ages. Both frequent and occasional smoking and drinking adversely affect personal and population health<sup>4</sup>. We show the adverse effect of both occasional smoking and drinking of alcohol upon poor HRQoL, which is critical information for public education. Thirdly,

differing from other studies<sup>18–23</sup>, our study categorized quality of life. This decision makes results more reliable, clearer, and more easily interpretable. Fourthly, also differing from other studies, our study delineated and adjusted for the relative impact of both individual and contextual variables upon poor HRQoL. This action enhances the credibility of the findings. Finally, our study used multivariable analyses that combined individual-level with regional-level data in order to avoid ecological and atomistic fallacies<sup>4</sup>. The preceding strengths of the study buttress the validity of the positive association between smoking and poor HRQoL and a possible causal linkage for this association. As in most studies, especially population-based studies<sup>18–23</sup>, our study focuses on the association between overall current smoking status (smoking/no smoking) and HRQoL. In order to obtain more detailed evidence about this issue, it will be necessary to further explore the relationship between smoking habits and poor HRQoL taking into account such variables as the quantity of smoking, smoking cessation, smoking initiation, ex-smoker, smoking duration, and others.

## Limitations

The study has limitations. First, our cross-sectional study design is an important research limitation and precludes the establishment of causal links between smoking and poor HRQoL. Nonetheless, we employed a large sample, and our findings met several criteria for inferring causality, including the strength of some associations, consistency between individual-level and contextual effects, and consideration of individual and contextual confounding and the biological plausibility of effects. Future studies need to collect longitudinal surveillance data on the HRQoL of university students. Secondly, another study limitation is that our respondents were health-profession students studying at universities. Consequently, our results are not generalizable to other populations or to the wider Chinese population. Thirdly, other studies that utilized the Chinese EQ-5D have not reported on internal reliability. This is the most basic indicator for evaluating the reliability of a questionnaire or scale. In our study, the Cronbach alpha coefficient of the EQ-5D only reached 0.56. This value emanated from a large sample—it would be less in small samples. Further research

is necessary. Finally, although the distribution of our sample of universities and colleges is consistent with the total distribution across the country, medical and other health-profession education in China is complex. They exist either as a college (or department) of medicine within a comprehensive university or as an independent medical institution under the central or local jurisdiction; thus, our sample representation is limited. The impact of this organizational complexity on our research questions warrants in-depth investigation.

## Implications

Many studies have confirmed that smoking is causally associated with various diseases, and some studies have found an association between smoking and human functional impairment. This study examined the association between smoking and poor HRQoL in university settings across China. The study provided additional evidence that smoking is harmful to health, such as the adverse effect of both occasional smoking upon poor HRQoL, but more importantly, helps to elucidate the smoking risk mechanism. This study suggests the importance of the enforcement of public tobacco control education and policy to better protect people from the harms of smoking in China.

## CONCLUSIONS

This study offers formidable evidence that smoking is associated with poor HRQL. Findings in this study of younger people underscore the importance of alerting the populace that functional impairment is linked to smoking. It will be necessary to implement stronger tobacco control and public education campaigns across China, and important to fortify public education programs among university students and reinforce a tobacco-free campus so as to diminish their tobacco use.

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#### CONFLICTS OF INTEREST

The authors have each completed and submitted an ICMJE form for disclosure of potential conflicts of interest. The authors declare that they have no competing interests, financial or otherwise, related to the current work. T. Yang and I.R.H. Rockett report that since the initial planning of the work, payments were received from Global Bridges/IGLC (2014SC1, 13498319) and Zhejiang University Education Fund (R0408).

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#### ETHICAL APPROVAL AND INFORMED CONSENT

The study was approved by the Ethics Committee at the Zhejiang University Medical Center (Approval number: 2014-1-017; Date: March 2014). Verbal informed consent was obtained from all participants before data collection.

#### DATA AVAILABILITY

The data supporting this research are available from the authors on reasonable request.

#### AUTHORS' CONTRIBUTIONS

TY conceived the study design, conceptualized the ideas, and supervised the data management and analyses. SP and DW conducted the data collection. TY and IRHR revised and edited the manuscript. All authors reviewed earlier drafts and approved the final version.

#### PROVENANCE AND PEER REVIEW

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