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Associations of long-term exposure to ambient air pollution and physical activity with insomnia in Chinese adults

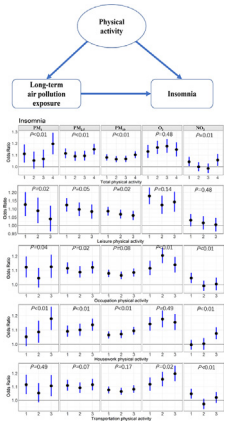
Jiayue Xu [a,1], Junmin Zhou [a,1], Peng Luo [b], Deqiang Mao [c], Wen Xu [d], Qucuo Nima [e], Chaoying Cui [f], Shujuan Yang [a], Linjun Ao [a], Jialong Wu [a], Jing Wei [g], Gongbo Chen [h], Shanshan Li [i], Yuming Guo [i], Juying Zhang [a,*], Zhu Liu [j,*], Xing Zhao [a,*], on behalf of the China Multi-Ethnic Cohort (CMEC) collaborative group

[a] West China School of Public Health and West China Fourth Hospital, Sichuan University, China
[b] School of Public Health, the key Laboratory of Environmental Pollution Monitoring and Disease Control, Ministry of Education, Guizhou Medical University, Guiyang 550025, China
[c] Chongqing Municipal Center for Disease Control and Prevention, Chongqing 400042, China
[d] Yunnan Center for Disease Control and Prevention, Kunming 650022, China
[e] Tibet Center for Disease Control and Prevention CN, Lhasa 850000, China
[f] Tibet University, Lhasa 850000, China
[g] Department of Chemical and Biochemical Engineering, Iowa Technology Institute, Center for Global and Regional Environmental Research, University of Iowa, Iowa City, IA, USA
[h] Guangdong Provincial Engineering Technology Research Center of Environmental and Health Risk Assessment; Department of Occupational and Environmental Health, School of Public Health, Sun Yat-sen University, Guangzhou, Guangdong, China
[i] Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia
[j] Chengdu Center for Disease Control and Prevention, Chengdu 610041, China

HIGHLIGHTS

- Positive associations were observed for long-term exposure to PMs, O_3 and insomnia.
- Complex effect modifications were observed for specific physical activity (PA).
- Adequate leisure PA alleviates the harmful effects of air pollution on insomnia.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Air pollution is a potential environmental risk for sleep disturbance. However, the evidence is very limited in China. On the other hand, physical activity (PA) is a preventive behavior that can improve insomnia, but whether PA mitigates the negative impact of air pollution on insomnia is unknown.
Methods: We obtained data from the baseline of China Multi-Ethnic Cohort (CMEC) survey, and examined the association between air pollution and insomnia, as well as PA's modification effect of on this association. We included 70,668 respondents and assessed insomnia by self-reported symptoms collected using electronic

* Corresponding authors.
E-mail addresses: luopeng@gmc.edu.cn (P. Luo), aolinjun@stu.scu.edu.cn (L. Ao), chengb36@mail.sysu.edu.cn (G. Chen), Shanshan.Li@monash.edu (S. Li), yuming.guo@monash.edu (Y. Guo), juying109@163.com (J. Zhang), 137949813@qq.com (Z. Liu), xingzhao@scu.edu.cn (X. Zhao).
[1] Jiayue Xu and Junmin Zhou contributed equally to this work and should be considered co-first authors.

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questionnaires. Using satellite data, we estimated the residence-specified, three-year average PM_1, $PM_{2.5}$, PM_{10} (particulate matter with aerodynamic diameters of ≤1 μm, ≤2.5 μm and 10 μm, respectively), O_3 (ozone), and NO_2 (nitrogen dioxide) concentrations. We established the associations between air pollutants and insomnia through logistic regression. We evaluated the modification impact of total and domain-specific PA (leisure, occupation, housework, transportation) by introducing an interaction term.

Results: Positive associations were observed between long-term exposure to PM_1, $PM_{2.5}$, PM_{10}, and O_3 and insomnia symptoms, with ORs (95% CI) of 1.09 (1.03–1.16), 1.11 (1.07–1.15), 1.07 (1.05–1.10) and 1.15 (1.11–1.20), respectively. As total PA increased, the ORs of air pollution for insomnia tended to decrease and then rise. We observed varying modification effects of domain-specific PA. With an increase in leisure PA, the ORs for $PM_{2.5}$ and PM_{10} significantly declined. However, increased ORs of air pollutants were related to insomnia among participants with higher levels of occupational and housework PA.

Conclusion: Long-term exposure to higher concentrations of PM_1, $PM_{2.5}$, PM_{10}, and O_3 increases the risk of insomnia symptoms. Moderate to high levels of leisure PA alleviate the harmful effects of air pollution on insomnia, while high levels of occupation and housework PA intensify such effects.

1. Introduction

Insomnia—with the main symptoms being having difficulty falling asleep at night, waking up during the night, or waking up too early—is one of the most common sleep disorder in the world (Sateia, 2014; Léger et al., 2008). European surveys have shown that over 40% of the general population suffers from insomnia (Calem et al., 2012; Sundbom et al., 2013). The prevalence in China was approximately 36% as reported by the China Chronic Disease and Risk Factor Surveillance survey in which year (Yin et al., 2011). Numerous studies have found that insomnia is linked with many detrimental health outcomes, such as rheumatoid arthritis, myocardial infarction, coronary heart disease, and stroke (Sofi et al., 2014; Sivertsen et al., 2014). Insomnia is also a significant risk factor for several mental disorders, especially depression and anxiety (Sivertsen et al., 2014; Neckelmann et al., 2007).

Previous studies have shown that air pollution is a potential environmental risk factor for poor sleep quality, possibly due to its negative effects on the sleep-wake cycle and sleep-disordered breathing (Zanobetti et al., 2010; Lawrence et al., 2018; Chen, 2019; Wang et al., 2020; Liu et al., 2020). However, such evidence is limited in China, which is one of the most polluted countries in the world and with over 1.8 million air pollution-related premature deaths in 2019 (http://ghdx.healthdata.org/gbd-results-tool). Furthermore, previous studies tended to focus on specific populations (e.g., children and rural inhabitants), which limited their ability to extrapolate to general populations. Moreover, existing studies had focused on overall sleep quality and sleep latency, with limited data specifically on insomnia, which is more related to people's overall health , work performance and life quality (Roth, 2007).

Identifying effect modifiers—especially preventive modifiers—for the adverse health outcomes of ambient air pollution is important for intervention programs. Habitual physical activity (PA) was recognized to be beneficial for sleep health via increasing slow-wave sleep time, elevating body temperature in sleep and enhancing parasympathetic control etc. (Uchida et al., 2012a). However, as activity pattern and energy expenditure of occupational, transportation, housework, and leisure-time PA differ substantially, different domains of PA would exert different effects on sleep via different mechanisms (Morgan, 2003). For example, leisure PA could exert positive effect on sleep quality by improve fitness level and mood Uchida et al., 2012a. Otherwise, repetitive occupational PA is closely associated with musculoskeletal pain and psychological stress, which may lead to insomnia (Skarpsno et al., 2019). The evidence of association between insomnia with respect to different domains of physical activity is limited (Zheng et al., 2017), and their modification effects on association between air pollution and insomnia is lacking. Previous study indicated that moderate to high levels of Physical activity (PA) —regardless of total or domain-specific PA—are associated with lower risks of insomnia in Chinese adults (Zheng et al., 2017). However, PA may increase the ventilation rate, which increases the intake of air pollutants, thus aggravating air pollution's harmful effects on sleep health. Furthermore, different domain of PA may have different modification effect. This study hypothesized PA as a modifier and explores whether PA could attenuate the detrimental impact of air pollution on insomnia with its positive influence, or amplify it by augmenting exposure to air pollution, or have no modification effect (Guo et al., 2020; Hou et al., 2020; Cole-Hunter et al., 2016; Li, 2020). The directed acyclic graph of air pollution, insomnia and PA was shown in Fig. S1.

Using the baseline data of a newly established cohort study in Southwest China, we aim to: 1) comprehensively evaluate the association of long-term exposure to ambient air pollutants—including PM_1, $PM_{2.5}$, PM_{10} (particulate matter with aerodynamic diameters of ≤1 μm, ≤2.5 μm, and 10 μm, respectively), O_3 (ozone), NO_2 (nitrogen dioxide) — with insomnia in a large-scale population of multi-ethnic Chinese adults; 2) determine how total and domain-specific PA impact the relationship between ambient air pollution and insomnia.

2. Method

2.1. Data

We gathered the data from the baseline of the China Multi-Ethnic Cohort (CMEC) survey, conducted in five provinces in Southwest China. The CMEC is supported by the National Key Research & Development Program of China aiming to examine the national ethnic variation in non-communicable diseases. It was administered from May 2018 to September 2019 and sampled 99,556 participants from seven ethnic groups (Han, Tibetan, Yi, Miao, Bai, Bouyei and Dong). A multistage, stratified cluster sampling method was applied to get samples from community-based populations. In the first stage, one to two minority settlements for each ethnic group were selected as our study sites. In the second stage, one to eight communities (depending on the size of communities) in each settlement were selected by the local Centers for Disease Control and Prevention (CDCs), considering migration status, local health conditions and, most importantly, ethnic structure. In the final stage, participants who met our inclusion criteria were invited to participate in our studies in consideration of both sex ratio and age ratio. Electronic questionnaires and health exams were mainly applied to collect participant data, including demographic and socioeconomic details, health behaviors, disease history, mental health status, and insomnia symptoms. Information related to the CMEC is described in the cohort profiles (Zhao et al., 2020).

We did not include Tibetan residents in Aba or Lhasa in our study ($n = 4992$ for Aba; $n = 7737$ for Lasa). They reside at high altitudes and live in a hypoxic environment where living habits (including PA and sleep) differ vastly from their counterparts at low altitudes (Bloch et al., 2015; Merrill, 2020). In addition, Tibetans in Aba are herdsmen

and their place of residence changes with the season. We also excluded participants if they 1) had unavailable addresses ($n = 31$); 2) had lived at their current residence for less than 3 years ($n = 9376$); 3) were pregnant ($n = 211$); 4) had tuberculosis and were taking medicine ($n = 544$); or 5) had a history of mental illness ($n = 313$), neurasthenia ($n = 1206$), pulmonary heart disease ($n = 415$), traumatic brain injury ($n = 2016$), or cancer ($n = 785$). We also excluded those with missing information on insomnia symptom metrics. We ended up including 70,668 participants in our study (Fig. 1), for which we received approval from the Sichuan University Medical Ethical Review Board (K2016038).

2.2. Insomnia symptoms

The CMEC contains subscales to assess sleep quality and PA. Among the sleep quality metrics, three insomnia symptoms were measured over the past month, including 1) having difficulty falling sleep at night (≥30 min) for 3 or more days a week; 2) waking up too early and having difficulty falling in sleep again for 3 or more days a week; and 3) having to take medicine to get to sleep for 1 or more days a week. If a participant answered 'yes' to any of those three questions, we classified him/her as having insomnia symptoms. We based the cut-offs for insomnia on the Diagnostic and Statistical Manual of Mental Disorders (DSM—V) (Abbas and Mahin, 2013).

2.3. Air pollution

Wei et al. estimated ambient air pollution concentrations from 2015 to 2019 using the space-time extremely randomized trees (STET) model (Wei et al., 2019a, 2020, 2021a, 2019b, 2021b). Combined with satellite-derived aerosol optical depth (AOD) and ground-based monitoring data, the tree approach simulated 1 km × 1 km resolution of PM_1, $PM_{2.5}$ and PM_{10} with 10-fold cross-validation R^2s of 0.86, 0.89, and 0.77, respectively. O_3 and NO_2 with a 25 km × 25 km resolution were generated with 10-fold cross-validation R^2s of 0.84 and 0.72, respectively.

Residence locations were geocoded with Gaode and Baidu maps. Estimated annual ambient PM2.5 concentrations were mapped to participants in the corresponding address. Average air pollution concentrations for the three years prior to the time of the investigation were calculated as individual exposure.

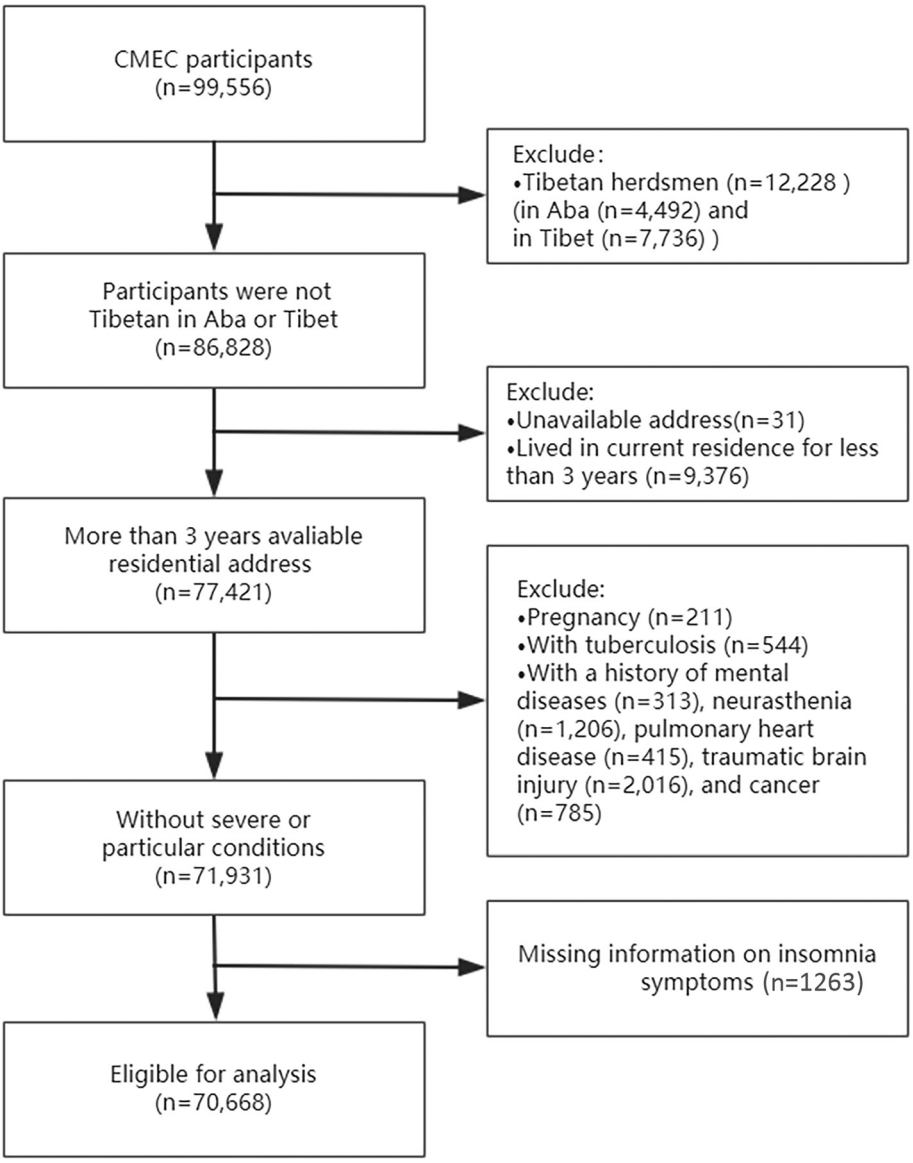

Fig. 1. Flowchart for participants selection.

2.4. Covariates

Potential confounding covariates include health behaviors, demographic and socioeconomic information, health-related variables and environmental factors.

Health behaviors include PA. Domain-specific PA in the past year was evaluated using a questionnaire based on an existing validated questionnaire that has been widely employed in PA surveys administered to different populations, including the Chinese population (Matthews et al., 2003; Wareham et al., 2002; Du et al., 2013). The CMEC PA questionnaire was further adapted after the pilot study. The participants were asked about their usual activities and duration during the past year regarding occupation, transportation, housework, and leisure-time exercise. Metabolic equivalent tasks (METs) were harnessed to quantify the amount of PA (Ainsworth et al., 2011). The MET value was the ratio of energy expended by an individual for 1 h of activity compared to 1 h of sedentary activity, so a 1-hour sedentary behavior equaled 1 MET. The MET score for each day of the activity is the MET value of the activity multiplied by the number of hours per day it lasts. The total and domain-specific PAs are the summation of the corresponding MET scores. In addition, cooking behavior, fuel type, and ventilation system were integrated into one variable and included as a proxy of indoor air pollution level. Indoor air pollution was grouped into three levels (low: little or no cooking at home; moderate: cooking at home using clean fuel or unclean fuel with ventilation equipment; high: cooking at home using unclean fuel without ventilation equipment). Health behaviors also include smoking status (never smoked, quit smoking, or currently smoking), secondhand smoke exposure (yes or no), the Mediterranean Diet Pattern (MED) score (Fung et al., 2005) and frequency of tea consumption (never, occasionally: 1–2 times a week; often: 3 or more times a week).

Demographics encompassed age, sex, ethnicity (Han or minority), residential province. Socioeconomic status was reflected by educational attainment (no normal education, primary school, junior school, junior high school, high school or junior college and above) and annual family income (<12,000 yuan, 12,000–19,999 yuan, 20,000–59,999 yuan, 60,000–99,999 yuan or ≥100,000 yuan). Health-related variables included body mass index (BMI) categories (<24, 24–27.9 or ≥28 kg/m^2), self-assessed health status (bad, moderate or good), self-reported physical pain or discomfort rating (ranging from 1 to 5; 1 = no pain or discomfort and 5 = severe pain or discomfort), and symptoms of anxiety and depression (yes-no questions). Environmental factors included temperature, relative humidity and the surrounding greenness of the residence. Three-year average level of all environmental factors in resident address was calculated corresponding to the air pollution. Residential greenness was gauged via the Moderate Resolution Imaging Spectroradiometer (MODIS) Terra Normalized Difference Vegetation Index (NDVI) at a spatial resolution of 500 m. The value of the NDVI ranges from −0.2 to +1.00, with a higher value denoting greater greenness cover.

2.5. Statistical analysis

We used descriptive and univariate variable analyses. Multivariate natural cubic spline regression and logistic regression were applied to test the association between air pollutants and insomnia after adjustment for potential confounders. The final model included seventeen covariates (age, sex, annual family income, education level, ethnicity, resident's province, smoking status, secondary smoke, indoor air pollution, PA, MED score, BMI, self-assessed health, pain rating, temperature, humidity and neighborhood greenness). The logistic regression model was adjusted for total and domain-specific PA separately. We evaluated the modifying effect of total PA and domain-specific PA on the association between air pollution exposure and insomnia using an interaction term, with the significance tested via the likelihood ratio test. For the interaction analysis, total PA was transformed into four categories (<11.7, 11.7–21.9, 22.0–37.2 or >37.2 METs/day) according to its quartiles. Occupation, housework and transportation were transformed into three categories (<3.7, 3.8–21.7 or >21.7 METs/day for occupation; <2.8, 2.9–5.6, >5.6 METs/day for housework; 0, 0.1–1.75, >1.75 METs/day for transportation) according to their tertiles. Since over half of the participants reported no leisure PA, we transformed it into three categories: never (0 METs/day), low (0.1–3.3 METs/day), and high (>3.3 METs/day). The cutoff value for low and high levels of leisure PA was its 75% quantile.

We conducted additional stratified analyses to examine the modification effect of age (<60 and ≥60), sex (male and female), ethnicity (Han and minority), BMI (< 24, 24–27.9 and ≥28 kg/m^2), and smoking status (never smoked, quit smoking, or currently smoking).

We also carried out several sensitivity analyses. 1) We tested the associations between air pollutants and insomnia symptoms using an alternative definition of insomnia that encompasses symptoms of having difficulty falling asleep at night, waking up too early in the morning and finding it hard to get to sleep again, and being unable to remain sober-minded during the day because of poor sleep (Zheng et al., 2017). 2) We tested the associations between air pollutants and insomnia symptoms using concentrations of different exposure windows (one year, two years, and four years). 3) We constructed a two-pollutant model to adjust for the confounding effect of gaseous pollutants on particulate matter and vice versa. 4) We included residents in Lhasa to test the association.

3. Results

3.1. Exposure distribution and insomnia prevalence

Overall, we included 70,668 participants whose insomnia prevalence was 42.1%. We selected them from six ethnic groups, the majority being Han Chinese (63.8%). Their average age was 55.2 years old, with a three-year average exposure concentration of 28.4 μg/m^3 for PM_1, 42.4 μg/m^3 for $PM_{2.5}$, 72.8 μg/m^3 for PM_{10}, 77.9 μg/m^3 for O_3, and 22.6 μg/m^3 for NO_2. Air pollution varies extensively among regions, being lower in Yunnan and Guizhou, and higher in Sichuan and Chongqing (Fig. S2). Compared with non-insomniacs, insomniacs tended to be exposed to higher PM_1, $PM_{2.5}$ and PM_{10} concentrations, and lower O_3 concentrations (Fig. 2). The exposure concentrations of NO_2 were close between the two groups (Fig. 2).

3.2. The participants' basic characteristics

Table 1 outlines the participants' basic characteristics. The mean age of those with insomnia symptoms was older than that of participants

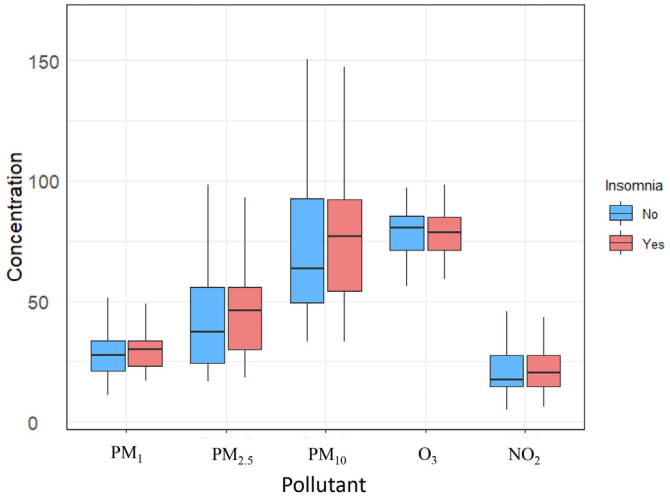

Fig. 2. Comparison of Exposure Distribution between Participants with Insomnia Symptoms and without.

Table 1
Comparison of sociodemographic data and major risk factors between participants with and without insomnia.

Variable	Insomnia			P-value
	Total ($n = 70,668$)	No ($n = 40,940$)	Yes ($n = 29,728$)	
Age, years: mean (SD)	52.2 (11.4)	50.9 (11.3)	53.9 (11.2)	<0.001
PA, METs/day: mean (SD)				
Total	26.8 (18.3)	27.0 (18.1)	26.6 (18.7)	0.001
Leisure	1.9 (3.3)	1.9 (3.2)	1.9 (3.4)	0.013
Transportation	1.6 (2.1)	1.6 (2.1)	1.6 (2.2)	0.848
Housework	6.2 (6.2)	6.0 (6.0)	6.5 (6.5)	<0.001
Occupation	17.2 (17.3)	17.6 (17.2)	16.6 (17.5)	<0.001
Sex: n (%)				
Male	28,120 (39.8)	17,146 (41.9)	10,974 (36.9)	<0.001
Female	42,548 (60.2)	23,794 (58.1)	18,754 (63.1)	
Ethnicity: n (%)				
Han	45,093 (63.8)	25,957 (63.4)	19,136 (64.4)	<0.001
Dong	5853 (8.3)	3188 (7.8)	2665 (9.0)	
Bouyei	4744 (6.7)	2728 (6.7)	2016 (6.8)	
Yi	5205 (7.4)	3030 (7.4)	2175 (7.3)	
Miao	4368 (6.2)	2342 (5.7)	2026 (6.8)	
Bai	5405 (7.6)	3695 (9.0)	1710 (5.8)	
Province: n (%)				
Guizhou	14,961 (21.2)	8256 (20.2)	6705 (22.6)	<0.001
Sichuan	17,285 (24.5)	10,375 (25.3)	6910 (23.2)	
Yunnan	19,969 (28.3)	12,774 (31.2)	7195 (24.2)	
Chongqing	18,444 (26.1)	9530 (23.3)	8914 (30.0)	
Others	9 (0.0)	5 (0.0)	4 (0.0)	
Education level: n (%)				
Illiteracy	16,281 (23.0)	8403 (20.5)	7878 (26.5)	<0.001
Primary school	18,008 (25.5)	10,040 (24.5)	7968 (26.8)	
Junior high school	19,424 (27.5)	11,500 (28.1)	7924 (26.7)	
High school	8820 (12.5)	5455 (13.3)	3365 (11.3)	
Junior college and above	8134 (11.5)	5541 (13.5)	2593 (8.7)	
Annual family income, ¥[a]: n (%)				
<12,000	12,257 (17.3)	6333 (15.5)	5924 (20.0)	<0.001
12,000–19,999	12,098 (17.1)	6672 (16.3)	5426 (18.3)	
20,000–59,999	25,618 (36.3)	15,021 (36.7)	10,597 (35.7)	
60,000–99,999	10,855 (15.4)	6597 (16.1)	4258 (14.3)	
≥100,000	9759 (13.8)	6272 (15.3)	3487 (11.7)	
Smoking status: n (%)				
Never smoked	52,373 (74.1)	29,854 (72.9)	22,519 (75.8)	<0.001
Quit smoking	3498 (4.9)	2014 (4.9)	1484 (5.0)	
Currently smoke	14,797 (20.9)	9072 (22.2)	5725 (19.3)	
Secondary smoke: n (%)				
No	34,222 (48.4)	20,169 (49.3)	14,053 (47.3)	<0.001
Yes	36,446 (51.6)	20,771 (50.7)	15,675 (52.7)	
Alcohol drinking status: n (%)				
Never	39,267 (55.6)	22,616 (55.2)	16,652 (56.0)	0.008
Occasionally	21,575 (30.5)	12,495 (30.5)	9080 (30.5)	
Often	9825 (13.9)	5829 (14.2)	3996 (13.4)	
Indoor pollution: n (%)				
Low	36,618 (51.8)	6926 (16.9)	4301 (14.5)	<0.001
Moderate	25,491 (36.1)	32,091 (78.4)	23,807 (80.1)	
High	8454 (12.0)	1918 (4.7)	1620 (5.5)	
BMI: n (%)				
<23.9	36,618 (51.9)	21,266 (52.0)	15,352 (51.7)	<0.001
24–27.9	25,491 (36.1)	14,734 (36.1)	10,757 (36.2)	
≥28	8454 (12.0)	4873 (11.9)	3581 (12.1)	
MED score: n (%)				
<6	13,944 (19.7)	7561 (18.5)	6383 (21.5)	<0.001
6–8	15,700 (22.2)	8842 (21.6)	6858 (23.1)	
9–10	17,195 (24.3)	9968 (24.4)	7227 (24.3)	
>10	23,776 (33.6)	14,540 (35.5)	9236 (31.1)	
Pain rate: n (%)				
1	45,177 (63.9)	28,459 (69.5)	16,718 (56.3)	<0.001
2	21,473 (30.4)	10,928 (26.7)	10,545 (35.5)	
3	2853 (4.0)	1137 (2.8)	1716 (5.8)	
4	1092 (1.5)	393 (1.0)	699 (2.4)	
5	45 (0.1)	11 (0.0)	34 (0.1)	
Self-assessed health: n (%)				
Good	32,881 (46.5)	22,192 (54.2)	10,689 (36.0)	<0.001
Moderate	30,646 (43.4)	15,929 (38.9)	14,717 (49.5)	
Bad	7105 (10.1)	2798 (6.8)	4307 (14.5)	

(continued on next page)

Table 1 (*continued*)

Variable	Insomnia			P-value
	Total ($n = 70,668$)	No ($n = 40,940$)	Yes ($n = 29,728$)	
Anxiety: n (%)				
No	66,386 (93.9)	39,538 (96.6)	26,848 (90.3)	<0.001
Yes	4280 (6.1)	1401 (3.4)	2879 (9.7)	
Depression: n (%)				
No	67,073 (94.9)	39,834 (97.3)	27,239 (91.6)	<0.001
Yes	3595 (5.1)	1106 (2.7)	2489 (8.4)	

PA: physical activity; RH: relative humidity; NDVI: normalized difference vegetation index; BMI: body mass index; MED: Mediterranean diet.
[a] $1.00 was equivalent to ¥6.62 in 2018 and ¥6.90 in 2019.

without insomnia symptoms. A total of 60.2% were female; they had a higher prevalence of insomnia symptoms than their male counterparts. Residents with insomnia symptoms were less educated than their peers without insomnia (46.7% vs. 55.0% for junior high school and above). Residents with insomnia had lower incomes than those without insomnia (61.7% vs. 68.1% for an annual family income ≥20,000 yuan). Smoking was reported less frequently by participants with insomnia, but secondary smoke was reported more frequently by those with insomnia (19.3% vs. 22.2% for smoking; 52.7% vs. 50.7% for secondary smoke). Alcohol consumption status was similar between participants with insomnia and without insomnia. Insomniacs tended to live with a higher level of indoor air pollution than non-insomniacs (85.6% vs. 83.1% for moderate or high indoor pollution). Participants with insomnia showed poorer adherence to the MED diet than their peers without insomnia (55.4% vs. 59.9% for a MED score ≥ median). Insomniacs reported higher pain ratings and worse self-assessed health than non-insomniacs (7.3% vs. 3.8% for a pain rating ≥ 3; 14.5% vs. 6.8% for poor self-assessed health). A higher share of insomniacs than non-insomniacs had co-occurring anxiety and depressive symptoms (9.7% vs. 3.4% for anxiety; 8,4% vs. 2.7% for depression). In terms of PA, participants with insomnia had lower overall levels of PA than their counterparts without insomnia. The insomnia group had higher levels of household PA than the non-insomnia group, but the insomnia group's work PA was lower than that of the non-insomnia group. Both groups had similar levels of leisure time PA and transportation PA.

3.3. The main effects of air pollution

We estimated the associations between ambient air pollutants and insomnia using both non-linear and linear models. As depicted in Fig. 3, except for NO_2, the associations between air pollutants and insomnia showed an approximately linear tendency. Due to the linear model's better interpretation, we extended our study based on the results of the linear model. After adjusting for covariates (Model 1), the prevalence of insomnia was significantly associated with PM_1, $PM_{2.5}$, PM_{10}, and O_3, but not NO_2. A 10 μg/m^3 increase in PM_1, $PM_{2.5}$, PM_{10}, and O_3 was associated with 9% (OR: 1.09; 95% CI: 1.03–1.16), 11% (OR: 1.11; 95% CI: 1.07–1.15), 7% (OR: 1.07; 95% CI: 1.05–1.10) and 15% (OR: 1.15; 95% CI: 1.11–1.20) higher probabilities of insomnia symptoms, respectively. The association remained robust after replacing total PA with domain-specific PA (Model 2). Table 2 portrays the results of the logistic regression model.

3.4. The modification effects of PA

There was a statistically significant modification effect of positive associations between any of the three PM pollutants and insomnia by total PA. The modification effect of total PA on the association between NO_2 and insomnia was also statistically significant, even though the main effect of NO_2 was non-significant. Trends in ORs for four air pollutants (PM_1, $PM_{2.5}$, PM_{10}, and NO_2) were similar with the increase in total PA. Levels 2 and 3 of total PA attenuated the positive associations between air pollutants and insomnia, but Level 4 of total PA amplified these associations. As leisure PA rose, the air pollution-associated ORs of insomnia tended to decline. This modification effect was statistically significant for $PM_{2.5}$ and PM_{10}. For occupational PA, high activity levels seemed to significantly increase the ORs of insomnia for PM_1, $PM_{2.5}$, and O3. Evaluated housework PA would significantly amplify the ORs of insomnia for PM_1, $PM_{2.5}$, PM_{10}, and NO_2. There were no significant modification effects of transportation PA for PM, but we observed higher ORs of insomnia for a 10 μg/m^3 increase in O_3 at higher levels of transportation PA. Fig. 4 portrays the results of the modification effects of PA.

3.5. Stratification and sensitivity analysis

The results, stratified by ethnicity, showed heterogeneity in the association between gaseous pollutants and insomnia symptoms among the Han and minority ethnic groups (Fig. S3). With sensitivity analysis, we found a consistent association between air pollutants and symptoms of insomnia (Table S1).

4. Discussion

Our study to comprehensively examine the association between long-term exposure to ambient air pollution and insomnia symptoms in the general adult population in China, and to systematically assess the modification impact of domain-specific PA on such associations. In this study, long-term exposure to higher concentrations of PM_1, $PM_{2.5}$, PM_{10}, and O_3 led to a greater risk of insomnia disorder. Further, we identified varying modification effects of domain-specific PA on the association between long-term air pollution exposure and insomnia symptoms. In particular, increased leisure PA and moderate levels of total PA can attenuate the positive association between PM and insomnia, while high levels of total and occupational PA can intensify the adverse influence of PM. In addition, a high level of occupational PA can exacerbate the harmful outcomes of O_3.

Several biological pathways underlie the possible mechanism f of air pollution's detrimental effect on insomnia. Sustained exposure to significant levels of airborne PM (especially $PM_{2.5}$ and PM_1) can cause it to enter the central nervous system (CNS) by translocation across the alveolar-capillary barrier and blood-brain barrier, or direct invasion through the olfactory nerve (Costa et al., 2020; Genc et al., 2012). Subsequent oxidative stress and inflammation affect the sleep-wake cycle (Pan et al., 2013). Moreover, PM and O_3 exert a negative impact on respiratory systems by causing inflammation and edema of respiratory cells (Morteza et al., 2016). This leads to obstruction of the upper airway, increasing the risk of apnea and hypoxia, which in turn affect sleep (Liu et al., 2020).

Evidence of the association between air pollution exposure and the risk of insomnia or other sleep disturbance symptoms is limited. A U.S. multicenter cohort study found that an interquartile range (IQR) increase in PM_1 (17.4 μg/m^3) contributes significantly to a 1.2% decrease in sleep efficiency (Zanobetti et al., 2010). A Boston longitudinal health survey reported that higher traffic-related air pollution is significantly associated with a decline in sleep duration (Fang et al., 2015). The evidence from developed countries of the association between air pollution and sleep disturbance was not entirely consistent. A study based on a

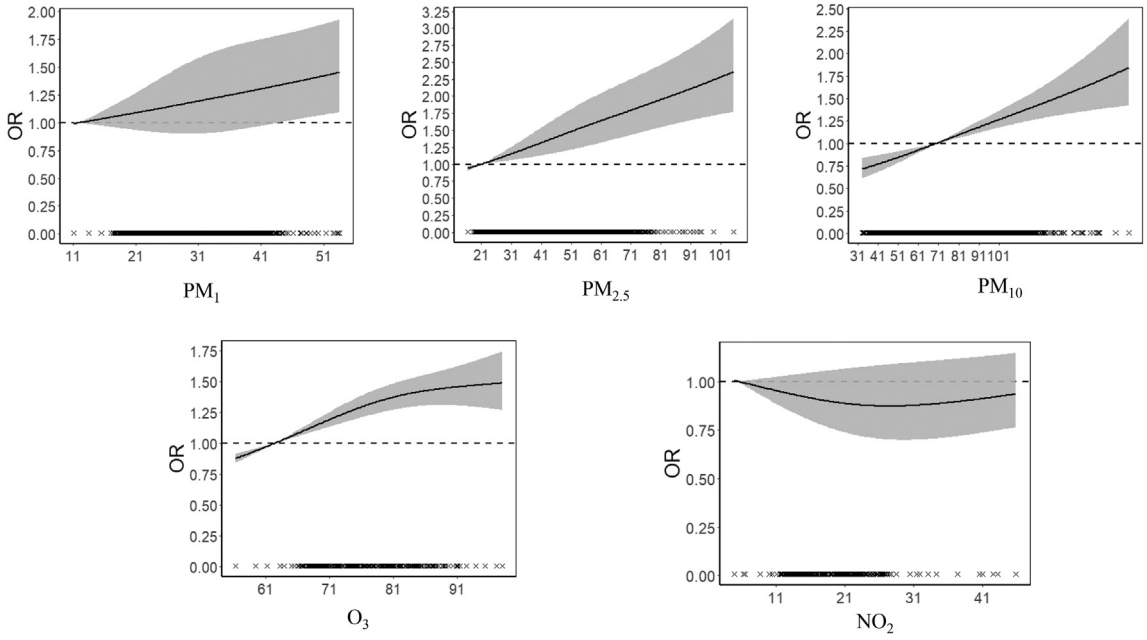

Fig. 3. Curve for odds ratios for the prevalence of insomnia associated with air pollutant (10 μg/m^3) spline.

Boston longitudinal health survey found a non-significant association between air pollution and sleep latency (Fang et al., 2015). However, a European multicenter cohort study revealed that traffic-related pollution is a potential risk factor for insomnia, defined as any symptoms of sleep latency, the inability to stay asleep, and waking up early in the morning (Janson et al., 2020). Current Chinese research has only been conducted among children and rural inhabitants. A Chinese study of 59,754 children from seven northeastern cities showed that an 11.6 μg/m^3 increase in concentrations of PM_1 and $PM_{2.5}$ was strongly tied to an elevated risk of sleep disorders (OR = 1.53, 95% CI: 1.38–1.69 for PM_1; OR = 1.47, 95% CI: 1.34–1.62 for $PM_{2.5}$) (Lawrence et al., 2018). A study grounded in a baseline survey of the Henan Rural Cohort found that the risk of poor sleep quality is significantly associated with per IQR increases in $PM_{2.5}$ (3.3 μg/m^3), PM_{10} (8.8 μg/m^3) and NO_2 (4.8 μg/m^3), with ORs (95% CIs) of 1.15 (1.03, 1.29), 1.11 (1.02, 1.21) and 1.14 (1.03, 1.25), respectively (Chen, 2019). A more recent study from the Henan Rural Cohort also suggested that the IQR increases in PM_1, $PM_{2.5}$, PM_{10} and NO_2 are positively associated with prolonged sleep latency, and with ORs (95% CIs) of 1.59 (1.33–1.90), 1.23 (1.13–1.33), 1.28 (1.13–1.45) and 1.43 (1.22–1.67), respectively (Wang et al., 2020). Similar to a previous investigation, we found a positive association between PM_1, $PM_{2.5}$, PM_{10} and insomnia in China's general adult population. The ORs of our study were smaller than those of preceding research for three main reasons: 1) The study populations were different. Since we included young and middle-aged adults, and they tended to be healthier, such effects may have been diminished. 2) The average concentration and range of air pollution exposure varies from study to study. Existing investigations in China have been performed in highly polluted areas with limited variability of exposure, and the air pollution in Western countries is generally low. 3) The adjustment of indoor air pollution differs across studies. Unclean fuel is still used in China and is a major contributor to indoor air pollution. Past studies in China have controlled for household fuel type or did not adjust for indoor pollution at all. In this study, in order to adjust for the effects of indoor air pollution, we synthesized information from three factors—the type of indoor fuel, the frequency of its use, and the ventilation system involved—that have a large influence on indoor pollution.

Table 2
Crude and adjusted odds ratios estimated by logistic regression for the prevalence of insomnia associated with air pollutants (10 μg/m^3).

Air pollutants	OR (95%CI)		
	Crude model	Model 1[a]	Model 2[b]
PM_1	1.15 (1.12–1.17)**	1.09 (1.03–1.16)*	1.09 (1.03–1.16)*
$PM_{2.5}$	1.06 (1.05–1.07)**	1.11 (1.07–1.15)**	1.11 (1.07–1.15)**
PM10	1.03 (1.03–1.04)**	1.07 (1.05–1.10)**	1.07 (1.05–1.10)**
O_3	0.91 (0.90–0.93)**	1.15 (1.11–1.20)**	1.15 (1.11–1.20)**
NO_2	1.01(1.00–1.03)	1.02 (0.99–1.05)	1.02 (0.99–1.05)

[a] Adjusted for age, sex, annual family income, education level, ethnicity, resident's province, smoking status, secondary smoke, indoor air pollution, total PA, MED score, BMI, self-assessed health, pain rating, temperature, humidity and neighborhood greenness.
[b] Same as Model 1, but replacing total PA with four domain-specific PA (leisure, occupation, housework and transportation).
* $p < 0.05$.
** $p < 0.001$.

We found mixed modifying effects of different intensities and categories of PA on the association between air pollution and insomnia. Our results signal that moderate or high levels of leisure PA can alleviate PM's negative impact on insomnia. This may be partially corroborated by a study based on half a million Chinese adults, implying that a moderate level of PA is associated with a lower risk of insomnia (Zheng et al., 2017). PA's beneficial effect on sleep is conceivable based on several mechanisms, which intersect with the biological pathways of air pollution. First, chronic PA could enhance antioxidant enzyme capacities and the inflammatory response by potentiating anti-inflammatory cytokines (Mury et al., 2018). Meanwhile, regular PA stimulates the release of brain-derived neurotrophic factor and growth hormones that are associated with longer, slower waves in the sleep-wake cycle (Uchida et al., 2012b). Other proposed mechanisms include body temperature changes, CNS fatigue, and improved fitness level (Uchida et al., 2012b; Kredlow et al., 2015). Therefore, regular PA could lower oxidative stress and affect CNS function, which would hedge against the negative health outcomes of air pollution on insomnia. However, a high level of occupation or housework PA aggravates air pollution's impact on insomnia. Although the underlying mechanism is still unclear, there is abundant evidence that occupational PA is associated with many harmful health effects including hypertension, myocardial infarction, and mental illness (Holtermann et al., 2012; Clays et al., 2014; Climie et al., 2019; Cillekens et al., 2020). In addition, a high level of occupational PA is closely tied to high job stress, which is a critical risk factor for insomnia (Yang et al., 2018). Like occupational PA, housework PA includes more static physical

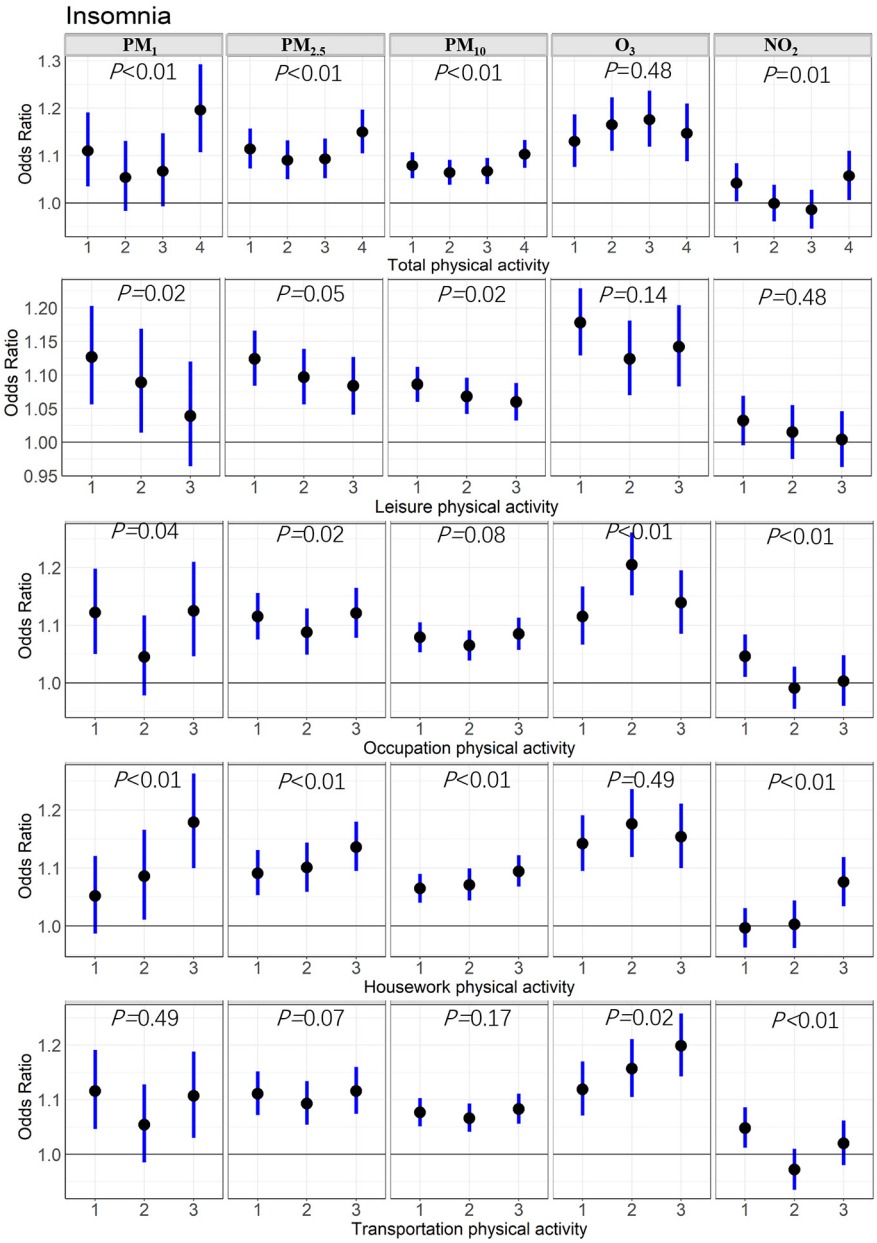

Fig. 4. Associations between air pollutants and insomnia symptoms for stratified participants with different levels of PA, *p*-values for examine the difference among stratified groups were calculated using likelihood ratio test.

activities of longer duration without enough rest. When doing housework, individuals do not intend to regularly engage large muscle groups with high intensity and obtain sufficient recovery. In addition, too much housework can cause stress. Thus, the health benefits of occupation and housework PA are limited and may be detrimental to health when overloaded.

This study has several strengths. First, the cohort's gradient exposure concentrations are advantageous for constructing an exposure-response function between air pollution and insomnia. Second, this study was based on a dataset with a large sample size and a wide range of covariates, which ensures the validity of the results. Third, we excluded residents who had lived at their current residence for less than 3 years, thereby improving the exposure misclassification. Fourth, we identified individuals with insomnia symptoms at the time of the investigation and excluded participants with pre-existing conditions that may have affected sleep. Thus, exposure is likely to precede the onset of insomnia.

Some limitations should be noted. First, the data come from the baseline survey of the CMEC; hence, causal inferences cannot be made. However, to avoid reversing cause and effect, we excluded those who had lived at their current address for less than 3 years and those who had a history of sleep-related conditions. Second, we did not measure individual caffeine intake, which is an important factor for sleep. Nevertheless, we used the frequency of tea (a universal source of caffeine intake in China) consumption as a proxy. Third, this study was based on a sample from China with unique cultural norms and patterns of health behaviors. Therefore, caution should be taken when generalizing the findings to other regions. Fourth, the resolution of O_3 and NO_2 are 25 km × 25 km, which may not fine enough to match the residential ambient air pollution concentration. Fifth, residential ambient air pollution concentration was used as exposure level which may not reflect the actual individual exposure. And PA was self-reported, which may have measurement error.

5. Conclusion

Long-term exposure to PM_1, $PM_{2.5}$, PM_{10}, and O_3 is positively associated with insomnia symptoms in Chinese adults. PA has mixed

modification effects on the association between air pollution and insomnia. A moderate level of total PA and a moderate to high level of leisure PA mitigate air pollution's adverse impact on insomnia, while high levels of total and occupational PA intensify the influence. We quantitatively evaluated air pollution's health effects on insomnia and have added evidence for the development of environmental standards. We also scrutinized the modification effects of PA and have provided scientific support for the implementation of individual target intervention programs.

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CRediT authorship contribution statement

Jiayue Xu: Data curation, Methodology, Formal analysis, Visualization, Writing – original draft. **Junmin Zhou:** Investigation, Data curation, Methodology, Writing – review & editing. **Peng Luo:** Investigation. **Deqiang Mao:** Investigation. **Wen Xu:** Investigation. **Qucuo Nima:** Investigation. **Chaoying Cui:** Investigation. **Shujuan Yang:** Investigation. **Linjun Ao:** Validation. **Jialong Wu:** Validation. **Jing Wei:** Resources. **Gongbo Chen:** Conceptualization, Methodology, Writing – review & editing. **Shanshan Li:** Conceptualization, Methodology, Writing-review & editing. **Yuming Guo:** Conceptualization, Methodology, Writing – review & editing. **Juying Zhang:** Methodology, Supervision, Writing – review & editing. **Zhu Liu:** Investigation, Supervision, Writing – review & editing. **Xing Zhao:** Conceptualization, Methodology, Investigation, Validation, Supervision, Funding acquisition, Project administration, Writing – review & editing.

Declaration of competing interest

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

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2021.148197.

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