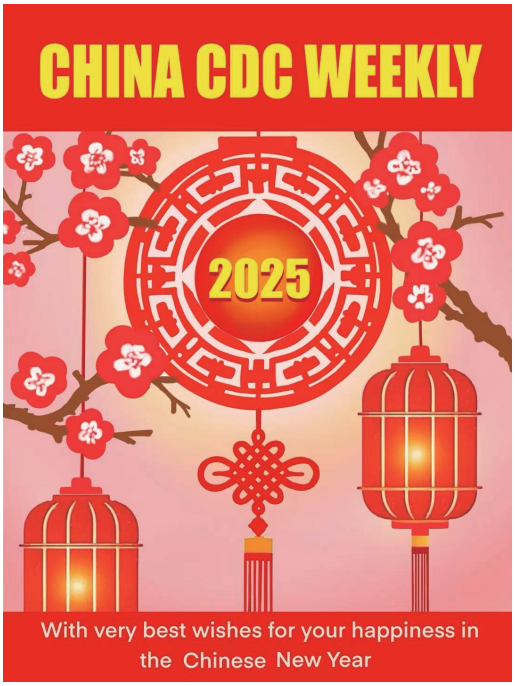
ISSN 2096-7071 (Print)
ISSN 2096-3101 (Online)
CN 10-1629/R1

CHINA CDC WEEKLY

Vol. 7 No. 5 Jan. 31, 2025

CDC weekly

中国疾病预防控制中心周报



Vital Surveillances

Preplanned Studies

ISSN 2096-7071
9 772096 707255 05>

Cover Image: credited from the designer Jiaying Wang.

Vital Surveillances

Evaluation of Integrated Service Strategy Based on Diagnosis of Duct-Dependent Congenital Heart Disease and Neonatal Mortality Data Analysis — Beijing, China, 2021–2022

Wen Zhang[1]; Zhengchao Chen[1]; Xiaozheng Chen[1]; Hongyan Xu[1]; Yanchun Zhang[1]; Kaibo Liu[1,#]

ABSTRACT

Objective: Integrated congenital heart disease (CHD) services were implemented in Beijing in 2022. This study analyzed prenatal diagnosis patterns and neonatal mortality data for duct-dependent CHDs before and after implementation to provide insights for service optimization.

Methods: We conducted a retrospective analysis of 487 cases of duct-dependent CHDs identified through the Beijing Birth Defects Monitoring System from January 2021 to December 2022. The study population included fetuses and infants from 13 weeks gestation to one year after birth. Cases underwent descriptive analysis focusing on disease occurrence, diagnostic timing, and mortality outcomes.

Results: The prenatal diagnosis rate for duct-dependent CHDs increased from 93.39% in 2021 to 93.91% in 2022, while delayed diagnosis rates decreased from 4.28% to 3.91%. Genetic diagnosis rates improved from 27.92% to 31.94%. Live birth rates following prenatal diagnosis increased substantially from 28.75% to 40.28%. Outcomes varied significantly by CHD subtypes, with complete transposition of the great arteries with intact ventricular septum achieving an 82.14% live birth rate, while hypoplastic left heart syndrome cases resulted in no live births. Notably, neonatal mortality decreased markedly from 7.23% to 3.03%.

Conclusions: Beijing's integrated service model for CHDs has effectively strengthened the connection between secondary and tertiary prevention strategies, reduced unnecessary pregnancy terminations, and improved neonatal survival outcomes.

Congenital Heart Defects (CHDs) represent the leading cause of birth defects and infant mortality worldwide (*1*). Among these, duct-dependent congenital heart defects constitute a particularly severe subset of CHDs that critically impact neonatal survival. These conditions are characterized by significant anomalies in systemic or pulmonary circulation that complicate the transition from fetal to postnatal circulation. Affected neonates depend heavily on systemic-pulmonary shunts, particularly the patency of the ductus arteriosus and foramen ovale, to maintain adequate systemic and pulmonary blood flow. Without intervention, ductal constriction occurring within hours to days after birth can precipitate severe cyanosis, circulatory collapse, or death. Early diagnosis coupled with prostaglandin E administration to maintain ductal patency postnatally has emerged as a crucial strategy for reducing neonatal mortality in these cases (*2*).

The etiology of duct-dependent CHDs is multifactorial, and effective primary prevention strategies remain elusive. Current clinical practice emphasizes secondary and tertiary prevention approaches, comprising mid-trimester ultrasound screening, neonatal physical examination with cardiac auscultation, and targeted echocardiographic evaluation following pulse oximetry screening when indicated. Beijing has maintained standardized prenatal ultrasound screening protocols since 2007, achieving coverage rates exceeding 95% (*3*). A significant advancement occurred in 2014 by incorporation right and left ventricular outflow tract views into prenatal ultrasound screening protocols, substantially improving the detection of complex CHDs. In 2022, Beijing implemented a comprehensive integrated service strategy for CHDs (*4*), establishing a coordinated network of prenatal diagnostic centers (n=10) that complete ultrasound consultations within 10 days, evaluating both cardiac and extracardiac malformations while investigating potential genetic etiologies. These centers collaborate with pediatric treatment facilities (n=5) through multidisciplinary consultations, providing evidence-based intervention recommendations for fetuses with severe, life-

threatening, or disabling conditions, thereby facilitating informed decision-making for pregnant women. For cases with well-defined treatment protocols and favorable postoperative outcomes, comprehensive counseling addresses disease progression, therapeutic options, prognosis, delivery hospital selection, and postnatal intervention strategies. This integrated prenatal screening and diagnosis model has maintained citywide ultrasound screening rates above 95% (*3*), with systematic referral pathways directing qualifying cases from screening institutions to prenatal diagnostic centers for definitive intrauterine diagnosis (*4*).

This study presents a retrospective analysis of duct-dependent CHDs diagnosis and neonatal mortality data in Beijing, comparing outcomes before and after the implementation of the integrated service strategy, with the aim of establishing baseline metrics and evaluating the effectiveness of current prevention and control measures.

METHODS

The birth defect surveillance system encompasses all maternity, induced labor, and pediatric institutions throughout Beijing. All CHDs diagnosed between 13 weeks of gestation and one year post-birth must be documented on birth defect registration cards, which capture comprehensive information including the infant's demographics, prenatal screening results, prenatal diagnosis details, and specific CHD subtype classification. In accordance with the "China Birth Defects Monitoring Program" (*5*), all Beijing medical institutions providing these services are designated as surveillance facilities and are mandated to complete registration cards for each confirmed case. Quality assurance measures include systematic medical record reviews, source document verification, cross-validation with perinatal and infant mortality databases, and follow-up investigations of unreported cases to ensure complete documentation.

The study population comprised late-term miscarriages, stillbirths, and live births from hospital deliveries or pregnancy terminations in Beijing. Data were extracted from the Beijing Birth Defects Hospital Surveillance Network across two distinct periods: pre- and post-implementation of the integrated service strategy. The pre-implementation period (January 1 to December 31, 2021) identified 257 fetuses/infants with duct-dependent CHDs among 147,305 perinatal cases. The post-implementation period (January 1 to December 31, 2022) documented 230 fetuses/infants with duct-dependent CHDs among 135,065 perinatal cases from the same surveillance network.

Patient follow-up was extended through the first year of life. To ensure accurate survival outcome tracking, particularly during the neonatal period, all cases underwent cross-verification against citywide infant mortality surveillance data, enabling comprehensive outcome assessment.

Diagnoses were established according to the International Classification of Diseases (ICD-11) (*6*). Prenatal diagnoses were confirmed exclusively through assessments conducted at designated prenatal diagnostic centers. The classification of duct-dependent CHDs (*2*) followed these distinct categories:

1) Systemic circulation disorder duct-dependent CHDs: These encompassed hypoplastic left heart syndrome, severe coarctation, and interrupted aortic arch;

2) Pulmonary circulation disorder duct-dependent CHDs: This category included tetralogy of Fallot, pulmonary atresia with intact ventricular septum, tricuspid atresia, and severe Ebstein's anomaly;

3) Other types of duct-dependent CHDs: This group comprised transposition of the great arteries with intact ventricular septum and total anomalous pulmonary venous return.

The timing of diagnosis was stratified into three distinct categories: prenatal diagnosis, early postnatal diagnosis (within 3 days of birth), and delayed diagnosis (≥3 days after birth) (*7*).

Statistical analyses were performed using IBM SPSS Statistics for Windows (version 19.0, IBM Corp., Armonk, NY, USA). The primary outcome measure was incidence rate, expressed in per mille (‰), which quantifies the frequency of duct-dependent CHDs in the study population and enables direct comparison between pre- and post-implementation periods of the integrated service strategy. Secondary outcome measures included prenatal diagnosis rate, genetic diagnosis rate, live birth rate following prenatal diagnosis, and neonatal mortality rate. These additional metrics provided comprehensive assessment parameters for evaluating the effectiveness of the integrated service strategy on duct-dependent CHD management and clinical outcomes.

RESULTS

The incidence rates of duct-dependent CHDs in

Beijing, including late-term miscarriages, stillbirths, and pediatric supplemental reports, were 1.74 ‰ (257/147,305) and 1.70‰ (230/135,065) before and after the implementation of the integrated service strategy, respectively.

Following the implementation of integrated services, several trends emerged in diagnostic patterns. The proportion of delayed diagnoses showed a modest decrease, while both prenatal and prenatal genetic diagnosis rates demonstrated slight increases. However, these changes did not reach statistical significance (delayed diagnoses: χ^2=0.042, P=0.839; prenatal and prenatal genetic diagnoses: χ^2=0.699, P=0.348), as detailed in Table 1. These findings suggest a trend toward earlier detection, although the differences remained statistically non-significant in our study population.

Following the implementation of the integrated services, referral rates for abnormal ultrasound screenings to prenatal diagnosis centers increased substantially from 60.61% in 2021 to 98.19% in 2022. The proportion of live births following prenatal diagnosis of duct-dependent CHDs rose to 41.20% (89/216), compared to 28.75% (69/240) before strategy implementation. Among cases undergoing invasive prenatal diagnosis, live birth rates increased from 24.24% to 40% following strategy implementation. Analysis by subtype, as shown in Table 2, revealed the highest survival rates for complete transposition of the great arteries with intact ventricular septum (82.14%, 23/28), followed by total anomalous pulmonary venous return (52%, 13/25), and moderate to severe aortic coarctation (45.65%, 21/46). No live births were recorded for hypoplastic left heart syndrome cases, reflecting its poor prognosis.

The proportion of duct-dependent CHD cases delivered in tertiary institutions increased from 83.13% to 89.9% following strategy implementation, with neonatal mortality rates decreasing from 7.23% to 3.03%. Statistical analysis using continuity-corrected χ^2 testing (χ^2=1.693, P=0.193) indicated that this difference in mortality rates was not statistically significant.

In 2022, three neonatal deaths occurred post-implementation, all involving isolated CHD cases. Two deaths resulted from protocol deviations: one case bypassed the mandated prenatal diagnostic center referral following abnormal screening, proceeding directly to pediatric consultation. This oversight resulted in missed extracardiac and genetic anomaly screenings, culminating in death 22 days post-surgery. The second case, lacking systematic prenatal care, led to delayed diagnosis following positive neonatal CHD screening and death 11 days before planned surgical intervention.

DISCUSSION

Over the past decade, Beijing's surveillance of CHD subtypes has generated data on critical CHDs that closely align with international benchmarks and accurately reflect population-level incidence (*8*). While most epidemiological studies of CHDs in China focus exclusively on perinatal outcomes, congenital cardiac defects can manifest throughout gestation (*9*). Severe cases may result in spontaneous miscarriage, intrauterine death, or therapeutic pregnancy termination, with the potential for missed diagnoses postnatally. Beijing has pioneered comprehensive CHD surveillance in China by including late-term miscarriages (13–27 weeks of gestation), stillbirths, and initial pediatric diagnoses in its monitoring period, thereby providing robust data on true CHD incidence and establishing a reliable foundation for assessing prevention strategies.

In this study, the prenatal ultrasound diagnosis rate for duct-dependent CHDs reached 93%, comparable to rates reported in developed nations (*10*). Following the implementation of the integrated service strategy, the referral rate of abnormal ultrasound screenings to

TABLE 1. Time of diagnosis and neonatal mortality of duct-dependent CHDs from 2021 to 2022.

Year	Occurrence	Time of diagnosis								Childbirth in tertiary institutions		Live birth	Neonatal death	
		Delayed diagnosis		Diagnosis within 3 days of birth		Prenatal diagnosis		Genetic diagnosis						
	No. of cases	No. of cases	Percentage (%)	No. of cases	Percentage (%)	No. of cases	Percentage (%)	No. of cases	Percentage (%)	No. of cases	Percentage (%)	No. of cases	No. of cases	Percentage (%)
2021	257	11	4.28	6	2.33	240	93.39	67	27.92	69	83.13	83	6	7.23
2022	230	9	3.91	5	2.17	216	93.91	69	31.94	89	89.9	99	3	3.03

Abbreviation: CHD=congenital heart disease.

TABLE 2. Incidence,diagnosis, and neonatal mortality of duct-dependent CHDs following the implementation of integrated strategies (case-based statistics).

Category	Subtype	Throughout pregnancy	Pediatric supplementary report	Total	Prenatal diagnosis		Diagnosis within 3 days of birth		Delayed diagnosis		Live birth	Neonatal death	
					No. of cases	Percentage (%)	No. of cases	Percentage (%)	No. of cases	Percentage (%)	No. of cases	No. of cases	Percentage (%)
Duct-dependent systemic circulation CHD	Hypoplastic left heart syndrome	18	0	18	18	100.00	0	–	0	–	0	0	0
	Interrupted aortic arch	10	0	10	9	90.00	1	10	0	–	4	0	0
	Severe aortic stenosis	47	2	49	46	93.88	2	4.08	1	2.04	24	0	0
Duct-dependent pulmonary circulation CHD	Tetralogy of Fallot	73	3	76	73	96.05	1	1.32	2	2.63	22	0	0
	Pulmonary atresia with intact ventricular septum	16	1	17	16	94.12	0	–	1	5.88	3	0	0
	Tricuspid atresia	4	1	5	4	80.00	0	–	1	20.00	1	1	100.00
	Ebstein's anomaly	10	0	10	10	100.00	0	–	0	–	4	0	0
Complete transposition of the great arteries with intact ventricular septum		28	1	29	28	96.55	1	3.45	0	–	24	1	4.17
Total anomalous pulmonary venous connection		25	4	29	25	86.21	0	–	4	13.79	17	1	5.88
Subtotal (Case-based statistics)		218	12	230	216	93.31	5	2.18	9	3.91	99	3	3.03

Abbreviation: CHD=congenital heart disease.
"–" means: "0".

prenatal diagnosis centers increased dramatically from 60.61% in 2021 to 98.19% in 2022, demonstrating significantly improved standardization of the referral process under the new protocol.

The prenatal genetic diagnosis rate increased modestly from 27.92% in 2021 to 31.94% in 2022, reflecting enhanced screening capacity and awareness of genetic factors. However, this proportion remains suboptimal, potentially due to families opting for pregnancy termination without genetic investigation when severe structural anomalies are detected. Precise prenatal ultrasound diagnosis of CHD subtypes is essential for prognostic assessment and informed maternal decision-making. Among those continuing pregnancies, the rate of invasive prenatal diagnosis increased from 24.24% to 40% following strategy implementation. The factors influencing acceptance of invasive prenatal diagnosis are likely multifaceted, encompassing procedural concerns and financial considerations, warranting dedicated investigation.

Following integration, the proportion of deliveries at tertiary institutions increased from 83.13% to 89.90%, while delayed diagnoses decreased from 4.28% to 3.91%. Current literature identifies non-tertiary hospital deliveries and delayed diagnosis of isolated cases as significant risk factors for adverse outcomes in critical CHDs (*11*). The integrated service strategy established robust obstetric-pediatric collaboration, resulting in nearly 90% of deliveries occurring at tertiary centers where prostaglandin E administration maintains ductal patency postnatally. Evidence suggests that optimized perinatal interventions reduce neonatal complications including distress, acidosis, intubation requirements, resuscitation needs, and emergency surgical interventions, thereby providing superior preoperative conditions for subsequent cardiac procedures (*12*). These interventions can significantly lower both preoperative and postoperative mortality rates in patients with transposition of the great arteries [95% confidence interval (*CI*): 0.06, 0.80; 95% *CI*: 0.01, 0.82] (*13*), potentially yielding improved long-term neurodevelopmental outcomes and quality of life (*14*).

Following the implementation of the integrated strategy, the live birth rate after prenatal diagnosis of duct-dependent CHDs increased from 28.75% in

2021 to 40.28% in 2022. For subtypes with established treatment protocols and favorable postoperative outcomes, particularly complete transposition of the great arteries with intact ventricular septum (*13*), the live birth rate following prenatal diagnosis increased markedly to 82.14% from 52.38% in 2021, substantially higher than previously reported rates of 22.79% (*15*). Conversely, in cases with poor prognosis, such as hypoplastic left heart syndrome (18 cases), families opted for pregnancy termination after comprehensive counseling. These preliminary findings suggest effective coordination between secondary and tertiary prevention under the integrated service strategy, with families of CHD patients with favorable prognoses more frequently choosing to continue pregnancies following thorough prenatal counseling.

The neonatal mortality rate for duct-dependent CHDs decreased from 7.23% in 2021 to 3.03% in 2022 after one year of strategy implementation. However, this difference did not reach statistical significance. Larger cohort studies with extended follow-up periods are necessary to definitively assess mortality trends in duct-dependent CHDs. Despite these initial promising outcomes, significant challenges remain in standardizing care protocols. Some institutions continue to deviate from established guidelines, either by bypassing prenatal diagnostic centers and referring cases directly to pediatric departments — potentially missing critical extracardiac malformations and genetic anomalies — or by providing inadequate follow-up for high-risk newborns after positive CHD screenings, resulting in delayed diagnoses and missed intervention opportunities. To address these issues, Beijing has initiated a specialized CHD infant mortality review process to refine referral criteria, enhance referral efficiency, and strengthen high-risk infant follow-up protocols, ensuring strict adherence to the integrated service strategy across all institutions to optimize treatment timing and further reduce infant mortality.

There were still some limitations. First, the study analyzed data from 2021 to 2022, with a sample size of 487 cases. Although this period covers the period before and after the implementation of the integrated service strategy, the sample size is relatively small and the time span is short, which may not fully reflect the long-term effects after the implementation of the strategy. Future studies may consider expanding the sample size and extending the observation period to obtain a more accurate and comprehensive assessment. Second, the study focused on changes in diagnostic patterns of duct-dependent congenital heart disease and neonatal mortality before and after the implementation of the integrated service strategy, but did not delve into other potential factors that may influence these outcomes. For example, economic status, preterm birth, low birth weight, distribution of medical resources and other factors. Future studies may incorporate these variables to more fully assess the effects of integrated service strategies.

In conclusion, Beijing's integrated strategy for congenital heart disease has successfully transcended traditional institutional boundaries, creating a comprehensive network that coordinates professional resources across the city's medical institutions. The strategy has evolved from institution-specific multidisciplinary cooperation to city-wide collaborative management, from risk stratification based solely on structural anomalies to comprehensive assessment incorporating genomic factors, and from reactive postnatal treatment to proactive integration of secondary and tertiary prevention. This systematic approach has effectively reduced unnecessary pregnancy terminations while decreasing neonatal mortality rates in the region.

Conflicts of interest: No conflicts of interest.

Funding: Supported by the National Key Research and Development Program of China (grant number 2018YFC1002304).

doi: 10.46234/ccdcw2025.025

[#] Corresponding author: Kaibo Liu, liukb@mail.ccmu.edu.cn.

[1] Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing Maternal and Child Health Care Hospital, Beijing, China.

Submitted: August 26, 2024
Accepted: November 28, 2024
Issued: January 31, 2025

REFERENCES

1. Zhang YY, Wang JY, Zhao JX, Huang GY, Liu KB, Pan W, et al. Current status and challenges in prenatal and neonatal screening, diagnosis, and management of congenital heart disease in China. Lancet Child Adolesc Health 2023;7(7):479 – 89. https://doi.org/10.1016/S2352-4642(23)00051-2.
2. Xia B, Zhang YQ. Pediatric ultrasound imaging handbook. Beijing: People's Medical Publishing House. 2018. https://book.kongfz.com/301245/7160653574. (In Chinese).
3. Zhang W, Xu HY, Zhang YC, Li DY, Liu KB. Epidemiological investigation of congenital hydrocephalus fetuses or infants and their

prognosis among surveillance period in Beijing. Chin J Obstet Gynecol Pediatr (Electron Ed) 2021;17(6):657 – 62. https://doi.org/10.3877/cma.j.issn.1673-5250.2021.06.006.
4. Beijing Municipal Health Commission. Notice on the Implementation of Integrated Services for Congenital Heart Disease，2022. https://wjw.beijing.gov.cn/zwgk_20040/zxgk/202202/t20220221_2613785.html [in Chinese].
5. National Office for Maternal and Child Health Surveillance. China Birth Defect Surveillance - Guidelines for Reporting Difficult and Minor Malformations (2012 Edition). https://www.mchscn.cn/BirthDefectMonitoring-25/417.html [in Chinese].
6. International Classification of Diseases Eleventh Revision (ICD-11). Geneva: World Health Organization; 2022. https://icd11.pumch.cn/ [in Chinese]
7. Olney RS, Ailes EC, Sontag MK. Detection of critical congenital heart defects: review of contributions from prenatal and newborn screening. Semin Perinatol 2015;39(3):230 – 7. https://doi.org/10.1053/j.semperi.2015.03.007.
8. Zhang W, Xu HY, Zhang YC, Liu KB. Epidemiological analysis of congenital heart disease in Beijing from 2017 to 2021. Chin J Obstet Gynecol Pediatr (Electron Ed) 2023;19(1):61 – 8. https://doi.org/10.3877/cma.j.issn.1673-5250.2023.01.009.
9. Zhang YL, Riehle-Colarusso T, Correa A, Li S, Feng XH, Gindler J, et al. Observed prevalence of congenital heart defects from a surveillance study in China. J Ultrasound Med 2011;30(7):989 – 95. https://doi.org/10.7863/jum.2011.30.7.989.
10. Bakker MK, Bergman JEH, Krikov S, Amar E, Cocchi G, Cragan J, et al. Prenatal diagnosis and prevalence of critical congenital heart defects: an international retrospective cohort study. BMJ Open 2019;9(7):e028139. https://doi.org/10.1136/bmjopen-2018-028139.
11. Liberman RF, Getz KD, Lin AE, Higgins CA, Sekhavat S, Markenson GR, et al. Delayed diagnosis of critical congenital heart defects: trends and associated factors. Pediatrics 2014;134(2):e373 – 81. https://doi.org/10.1542/peds.2013-3949.
12. Chakraborty A, Gorla SR, Swaminathan S. Impact of prenatal diagnosis of complex congenital heart disease on neonatal and infant morbidity and mortality. Prenat Diagn 2018;38(12):958 – 63. https://doi.org/10.1002/pd.5351.
13. Słodki M, Rizzo G, Augustyniak A, Seligman NS, Zych-Krekora K, Respondek-Liberska M, et al. Retrospective cohort study of prenatally and postnatally diagnosed coarctation of the aorta (CoA): prenatal diagnosis improve neonatal outcome in severe CoA. J Matern Fetal Neonat Med 2020;33(6):947 – 51. https://doi.org/10.1080/14767058.2018.1510913.
14. Bonnet D. Impacts of prenatal diagnosis of congenital heart diseases on outcomes. Transl Pediatr 2021;10(8):2241 – 9. https://doi.org/10.21037/tp-20-267.
15. Zhang W, Xu HY, Zhang YC, Liu KB. Delayed diagnosis of critical congenital heart defects predicting risk factors and survival rate in newborns in Beijing: a retrospective study. J Int Med Res 2021;49(7):3000605211028028. http://dx.doi.org/10.1177/03000605211028028.

Preplanned Studies

Ningxia First Case of *Orientia tsutsugamushi* Infection — Ningxia Hui Autonomous Region, China, 2023

Xiuxiu Li[1,&]; Dongyue Lyu[2,&]; Jian Li[3,&]; Jindong Zuo[1]; Hanyu Sha[2]; Liping Wang[1]; Xueping Ma[4]; Qun Duan[2]; Shuai Qin[2]; Ran Duan[2]; Rui Rao[1]; Deming Tang[5]; Ziyi Bu[6]; Lianxu Xia[2]; Huaiqi Jing[2]; Xin Wang[2,#]; Tao Zhang[4,#]

Summary

What is already known about this topic?

Scrub typhus is an acute infectious disease caused by *Orientia tsutsugamushi* that is transmitted primarily through the bite of infected chigger mite larvae. The disease prevalence is closely associated with environments characterized by high moisture levels and abundant vegetation.

What is added by this report?

This study documents the first confirmed case of scrub typhus in Ningxia Hui Autonomous Region, China. The patient presented with characteristic clinical manifestations, including abnormal biochemical indicators and positive serum-specific IgM antibodies against scrub typhus. Epidemiological evidence suggests local acquisition of the disease.

What are the implications for public health practice?

Enhanced surveillance and preventive measures for scrub typhus are essential in this region, particularly for individuals residing in or visiting areas where the disease may be endemic.

Scrub typhus, commonly known as Tsutsugamushi disease, is a natural-focal infectious disease caused by *Orientia tsutsugamushi*. The disease primarily circulates between rodents as reservoir hosts and chigger mite larvae as vectors, and remains the most underdiagnosed infectious disease globally. Clinical manifestations typically include acute onset, characteristic eschar or ulcers at the bite site, lymphadenopathy, and maculopapular rash (*1*). The disease is endemic throughout the Asia-Pacific region (including China, the Republic of Korea, Japan, and India), extends into northern Australia, and has emerged in Africa, southern Chile, and the Middle East (*2–3*). Here, this study reports the first documented case (2023) of *Orientia tsutsugamushi* infection identified in Ningxia Hui Autonomous Region, China.

A 58-year-old female farmer, who maintained livestock including cattle, sheep, and pigs near her residence along with domestic pets, presented with scrub typhus symptoms. Her home was situated in a hilly forested area surrounded by farmland with substantial rodent activity. The patient reported an insect bite on her right ankle on July 10, 2023, which developed into an itchy white rash that subsequently formed a scab after scratching. Three days post-bite, she experienced an acute onset of high fever (39.7 ℃) with accompanying headache, nausea, and localized inflammation at the bite site characterized by redness, swelling, itching, and pain. Though antipyretic medication reduced her temperature to 37℃, other symptoms persisted. Upon hospital admission on July 21, clinical examination revealed acute facial features, bilateral inguinal lymphadenopathy (right: 2.1 cm × 1.1 cm; left: 2.7 cm × 1 cm), and disseminated papular rash. The bite site displayed a small (0.15 cm), painful, black eschar on the medial aspect of the right ankle joint, surrounded by marked swelling (Figure 1). While Widal reaction and brucellosis tests were negative, laboratory findings showed decreased eosinophil (EO#), normal white blood cell (WBC) counts, and elevated hematocrit (HCT). Blood biochemistry revealed elevated C-reactive protein, increased myocardial enzymes, and elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT), indicating liver dysfunction (Table 1). Computed tomography confirmed bilateral inguinal lymphadenopathy (Table 1 and Figures 2A–B), supporting the scrub typhus diagnosis.

The therapeutic regimen consisted of: 1) intravenous levofloxacin sodium chloride (0.5 g, QD) for anti-infective treatment; 2) intravenous dexamethasone (5 mg) for anti-inflammatory effects; and 3) oral biphenyl diester (50 mg, TID) for hepatoprotection. Follow-up examination on July 28 demonstrated significant clinical improvement, with normalized laboratory parameters and a marked reduction in bilateral inguinal lymph node dimensions (right: 1.2 cm × 0.6 cm; left: 1.5 cm × 0.6 cm) (Table 1 and Figures

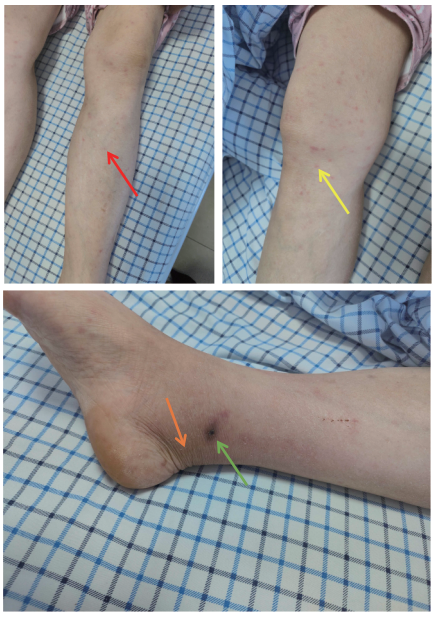


FIGURE 1. The changes in the skin of the patient after bite.
Note: Red arrow — early papules; yellow arrow — papules; orange arrow — swelling; green arrow — eschar.

2C–D).

Serum samples were collected from both the patient (August 16, 2023) and two local residents serving as controls. All samples underwent qualitative immunoassay analysis using Scrub Typhus Detect™ IgM and IgG ELISA Kits (InBios International, USA). Absorbance measurements at 450 nm were obtained using an ELx808 microplate reader (BioTek, USA). The patient's serum showed an IgM absorbance of 0.380, compared to control values of 0.068 and 0.067. IgG absorbance values were 0.048 for the patient and 0.023 and 0.036 for the controls.

Environmental investigation of the patient's residence yielded 33 captured rodents, comprising 12 *Mus musculus*, 12 *Spermophilus alaschanicus*, 6 *Meriones meridianus*, 1 *Allactaga sibirica*, 1 *Cricetulus barabensis*, and 1 *Rattus norvegicus*. From these rodents, 125 fleas and 10 mites were collected. The ectoparasites were homogenized, and nucleic acid was extracted using a Blood & Tissue Kit (69506, Qiagen, Hilden, Germany). Subsequent analysis using an *Orientia tsutsugamushi* Nucleic Acid Detection Kit (YJBI0145N Fluorescent PCR Assay) yielded negative results.

DISCUSSION

Scrub typhus is an acute infectious disease caused by *Orientia tsutsugamushi* infection that poses a significant public health challenge in the Asia-Pacific region. While laboratory diagnosis typically relies on serological testing (including Weil-Felix test and ELISA), false-negative results frequently occur during the acute phase. Consequently, diagnosis and treatment decisions often depend on clinical manifestations, which initially present as non-specific influenza-like symptoms (fever, headache, myalgia, and cough), followed by rash and characteristic eschar at the bite site, with potential progression to fatal outcomes in severe cases (*4*). The non-specific nature of scrub typhus symptoms creates diagnostic challenges, as they overlap with other acute febrile illnesses, including malaria, dengue fever, leptospirosis, and various Rickettsial diseases. The presence of eschar combined with relevant travel or residence history in endemic areas provides crucial diagnostic indicators. The patient presented with characteristic features, including acute onset following insect bite, fever, pruritic white rash, and a black eschar on the medial right ankle, aligning with both the epidemiological history and clinical presentation of scrub typhus, supporting the clinical diagnosis (*5*). Typical laboratory findings in scrub typhus patients include stable WBC counts with decreased or absent eosinophils, alongside liver function abnormalities marked by elevated AST and ALT levels. The patient's physical examination, computed tomography findings of bilateral inguinal lymphadenopathy, and blood biochemical profile demonstrated these characteristic features, with positive response to standard therapeutic protocols. While the patient's acute-phase serology showed positive IgM but negative IgG, similar serological profiles have been documented in previous case reports (*3*). Despite negative pathogen detection in environmental sampling around the patient's residence, the absence of travel history within 6 months prior to symptom onset strongly suggests local acquisition. The environment and vectors in the area will be under ongoing surveillance. Without appropriate treatment, scrub typhus can lead to severe complications, including hearing impairment and multiorgan failure, with case fatality rates varying regionally from 30% to 70% (*6*).

Scrub typhus predominantly occurs in the southwestern, southeastern coastal, and eastern regions of China, though its geographical distribution has recently expanded into northern regions (*7*). The disease exhibits distinct seasonality, emerging in May and reaching peak incidence during June and July, corresponding to weather patterns and mite life cycles.

TABLE 1. Biochemical test indicators of the case with scrub typhus.

Indicator	Before treatment	After treatment	Reference value
WBC (10^9/L)	4.8	7.8	3.5–9.5
NEUT# (10^9/L)	3.21	4.81	2–7
LYMPH# (10^9/L)	1.11	2.32	1.1–3.2
MONO# (10^9/L)	0.51	0.50	0.1–0.6
EO# (10^9/L)	0.01	0.10	0.02–0.52
BASO# (10^9/L)	0.00	0.02	0–0.06
NEUT (%)	66.3	62.1	40–75
LYMPH (%)	23.0	29.9	20–50
MONO (%)	10.5	6.5	3–10
EO (%)	0.2	1.3	0.4–0.8
BASO (%)	0.0	0.2	0–1
RBC (10^{12}/L)	5.95	5.43	3.8–5.1
HGB (g/L)	174	156	115–150
HCT (%)	52.6	48.2	35–45
AST (U/L)	75.89	31.56	13–35
ALT (U/L)	60.12	36.46	7–40
GTT (U/L)	51.34	40.46	7–45
Lactate dehydrogenase (U/L)	328.30	280.91	120–250
α-Butyrate dehydrogenase (U/L)	212.04	203.22	72–182
Inguinal lymph node sizes (cm)	Right: 2.1×1.1 Left: 2.7×1	Right: 1.2×0.6 Left: 1.5×0.6	–
High sensitivity C-reactive protein (mg/L)	25.50	6.22	0–3
PCT (ng/L)	0.54	–	<0.05

Note: "–" represents not available.
Abbreviation: WBC=white blood cell; NEUT#=neutrophi; LYMPH#=lymphocyte; MONO#=monocyte; EO#=eosinophil; BASO#=basophil; NEUT%=neutrophil ratio; LYMPH%=lymphocyte ratio; MONO%=monocyte ratio; EO%=eosinophil ratio; BASO%=basophil ratio; RBC=red blood cel; HGB=hemoglobin; HCT=hematocrit; AST=aspartate aminotransferase; ALT=alanine aminotransferase; GTT=γ-Glutamyl transpeptidase; PCT=procalcitonin.

Agricultural workers constitute a significant proportion of cases (*8*). The present case aligns with this epidemiological pattern, involving a farmer engaged in crop cultivation whose primary work environment encompasses farmland and grasslands. The patient's residential circumstances — maintaining livestock near her home amid a high density of rodent populations — created elevated risk conditions for exposure to infected chigger mites. Environmental investigation of the patient's living space serves multiple crucial purposes: tracing potential epidemiologic exposures, identifying possible pathogen reservoirs, and evaluating how rodent density in residential areas influences *Orientia tsutsugamushi* transmission. These insights are essential for developing targeted prevention and control strategies.

Currently, significant challenges in controlling scrub typhus include diagnostic delays and misdiagnoses, primarily due to insufficient clinician awareness. In this case, the patient's delayed healthcare-seeking behavior, combined with the limited diagnostic capabilities at the county hospital, prevented the collection of blood and eschar skin swab specimens for qPCR testing during the acute phase. Furthermore, the absence of local immunological testing facilities and standardized reagents, coupled with healthcare providers' limited awareness of scrub typhus, resulted in the failure to promptly report the case to the local CDC. Therefore, enhancing the detection and diagnostic capabilities of medical personnel is crucial. Physicians should synthesize laboratory findings with clinical manifestations and immediately report any suspected or confirmed cases of scrub typhus to the CDC, enabling rapid implementation of prevention and control measures to minimize transmission risk.

As the first reported case of scrub typhus in Ningxia Hui Autonomous Region, enhanced surveillance and preventive measures are crucial. While various

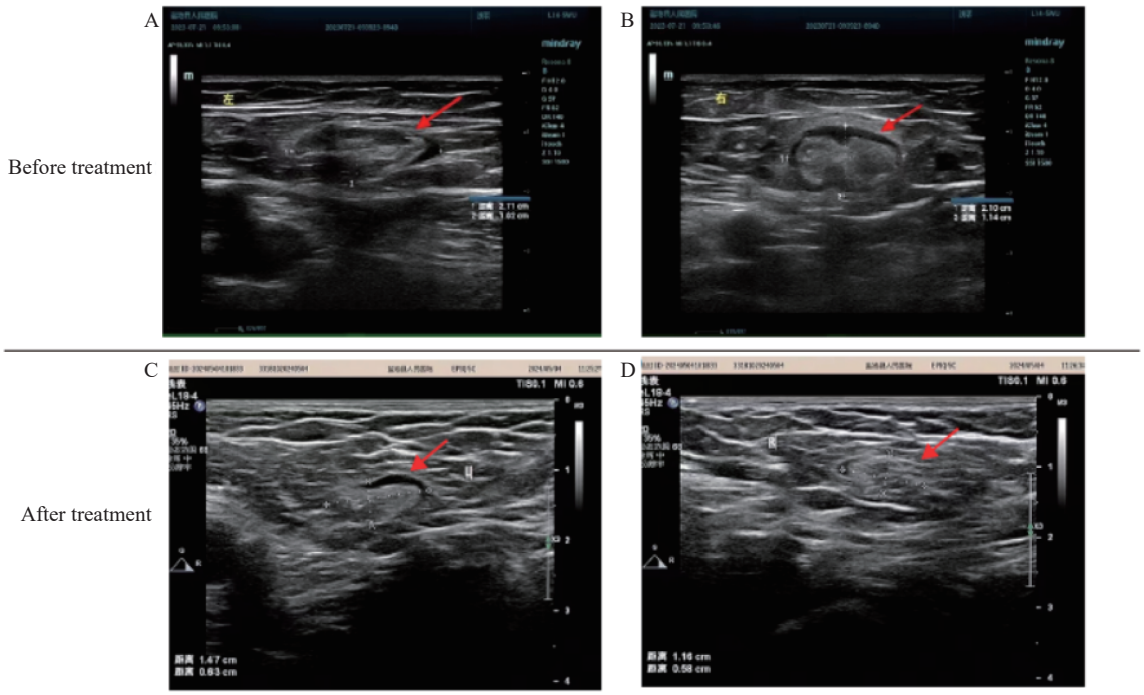


FIGURE 2. Computed tomography results of the case. (A) Left and (B) right inguinal lymph nodes before treatment; (C) Left and (D) right inguinal lymph nodes after treatment.

antibiotics are available for treatment, antimicrobial resistance remains a significant concern (*9*). Randomized clinical trials have demonstrated comparable efficacy among tetracycline, doxycycline, telithromycin, and azithromycin for treating scrub typhus (*10*). Azithromycin is particularly recommended due to its efficacy profile comparable to doxycycline (*11*). The World Health Organization (WHO) specifically recommends azithromycin or chloramphenicol for treating pregnant women and children due to their superior safety profiles. Ongoing research into drug resistance mechanisms is essential for developing new therapeutic strategies and understanding both treatment failures and pathogen resistance patterns. The absence of vaccines for Rickettsial diseases, including scrub typhus, presents a significant challenge, particularly given the substantial antigenic variation among *Orientia tsutsugamushi* strains, resulting in weak and transient cross-protection. This variation poses considerable obstacles to effective vaccine development. Successful management of Rickettsial diseases requires both prompt initiation of treatment upon clinical suspicion and implementation of robust preventive measures, especially for individuals in or traveling to endemic areas.

Conflicts of interest: No conflicts of interest.

Ethical approval: Approved by the ethics committee of the National Institute for Communicable Disease Control and Prevention of the Chinese Center for Disease Control and Prevention. Verbal informed consent was obtained from the patient.

Funding: Supported by the National Key Research and Development Program of China (2022YFC2602203).

doi: 10.46234/ccdcw2025.026

[#] Corresponding authors: Xin Wang, wangxin@icdc.cn; Tao Zhang, melody68man@163.com.

[1] People's Hospital of Yanchi County, Wuzhong City, Ningxia Hui Autonomous Region, China; [2] National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China; [3] Yanchi County Center for Disease Control and Prevention, Wuzhong City, Ningxia Hui Autonomous Region, China; [4] Ningxia Hui Autonomous Region Center for Disease Control and Prevention, Yinchuan City, Ningxia Hui Autonomous Region, China; [5] Dongcheng District Center for Disease Control and Prevention, Beijing, China; [6] Clinical College of Anhui Medical University, Hefei City, Anhui Province, China.
[&] Joint first authors.

Submitted: October 03, 2024
Accepted: January 17, 2025
Issued: January 31, 2025

REFERENCES

1. Biswas U, Ghosh R, Chakraborty A, Mondal SR, Roy D, Bhattacharjee A, et al. Cerebral venous sinus thrombosis following scrub typhus infection: a case report and a review of the literature. Med Res Arch 2022;10(10). http://dx.doi.org/10.18103/mra.v10i10.3196.
2. Ponnusamy L, Garshong R, McLean BS, Wasserberg G, Durden LA, Crossley D, et al. *Rickettsia felis* and other rickettsia species in chigger mites collected from wild rodents in North Carolina, USA. Microorganisms 2022;10(7):1342. https://doi.org/10.3390/microorganisms10071342.
3. Sun CB, Ma ZQ, Liu Z. Case report: optic neuritis as the initial presentation of *Orientia tsutsugamushi* infection detected by metagenomic next-generation sequencing. Front Immunol 2023;14:1129246. https://doi.org/10.3389/fimmu.2023.1129246.
4. Taylor AJ, Paris DH, Newton PN. A systematic review of mortality from untreated scrub typhus (*Orientia tsutsugamushi*). PLoS Negl Trop Dis 2015;9(8):e0003971. https://doi.org/10.1371/journal.pntd.0003971.
5. Society of Microbiology Committee on Zoonotic Pathogens Chinese, Technology Branch of China Medical Biotechnology Association Biodiagnostic. Expert consensus on the clinical diagnosis and treatment of scrub typhus. Chin J Zoonoses 2024;40(1):1 – 6. https://doi.org/10.3969/j.issn.1002-2694.2024.00.01.
6. Bonell A, Lubell Y, Newton PN, Crump JA, Paris DH. Estimating the burden of scrub typhus: a systematic review. PLoS Negl Trop Dis 2017;11(9):e0005838. https://doi.org/10.1371/journal.pntd.0005838.
7. Musa TH, Ahmad T, Wana MN, Li W, Musa HH, Sharun K, et al. The epidemiology, diagnosis and management of scrub typhus disease in China. Hum Vaccin Immunother 2021;17(10):3795 – 805. https://doi.org/10.1080/21645515.2021.1934355.
8. Luo L, Guo ZN, Lei Z, Hu QQ, Chen M, Chen FH, et al. Epidemiology of tsutsugamushi disease and its relationship with meteorological factors in Xiamen city, China. PLoS Negl Trop Dis 2020;14(10):e0008772. https://doi.org/10.1371/journal.pntd.0008772.
9. Lu CT, Wang LS, Hsueh PR. Scrub typhus and antibiotic-resistant *Orientia tsutsugamushi*. Expert Rev Anti Infect Ther 2021;19(12):1519 – 27. https://doi.org/10.1080/14787210.2021.1941869.
10. Lee SC, Cheng YJ, Lin CH, Lei WT, Chang HY, Lee MD, et al. Comparative effectiveness of azithromycin for treating scrub typhus: a PRISMA-compliant systematic review and meta-analysis. Medicine (Baltimore) 2017;96(36):e7992. https://doi.org/10.1097/md.0000000000007992.
11. Chanta C, Phloenchaiwanit P. Randomized controlled trial of azithromycin versus doxycycline or chloramphenicol for treatment of uncomplicated pediatric scrub typhus. J Med Assoc Thai 2015;98(8):756-60. https://pubmed.ncbi.nlm.nih.gov/26437532/.

Preplanned Studies

Association of Childhood Trauma Subtypes and Substance Use Among Chinese College Students — Jilin Province, China, 2021

You Wu[1,2,&]; Bowen Liu[3,4,&]; Leiyu Shi[1]; Dongyang Chen[3]; Yunhe Wang[5]; Dake Wei[6]; Diyang Qu[3]; Shicun Xu[7,8,9]; Yingjie Zhang[10,#]; Xiaoqian Zhang[4,#]

Summary

What is already known about this topic?

Childhood trauma represents a critical risk factor for substance use among young populations globally, presenting a substantial public health challenge.

What is added by this report?

This comprehensive investigation elucidates the distinct associations between specific subtypes of childhood trauma and substance use behaviors within the Chinese youth population. The findings demonstrate significantly elevated risks for smoking, e-cigarette use, and alcohol consumption, particularly among individuals who have experienced severe or multiple forms of childhood trauma.

What are the implications for public health practice?

Implementation of targeted interventions and support systems is essential for individuals with childhood trauma histories. Healthcare providers should emphasize early identification and trauma-informed care approaches. Policy frameworks promoting early intervention and sustained support mechanisms are crucial for reducing substance use behaviors and enhancing population health outcomes.

Substance use among college students represents a significant and growing public health challenge in China (*1*). Current data indicates cigarette use prevalence ranges from 7.8% to 13% among Chinese college students (*2*), while electronic cigarette use has shown an upward trend with rates between 3.1% and 5.5% (*3–4*). Alcohol consumption is particularly prevalent, with 34.2% to 49.3% of students reporting current alcohol use (*5*). Childhood trauma has emerged as a crucial determinant of substance use behaviors (*6*), encompassing distinct categories: emotional abuse (verbal assaults and intimidation), physical abuse (acts causing bodily harm), sexual abuse (traumatic sexual experiences causing psychological distress), emotional neglect (inadequate emotional support and nurturing), and physical neglect (insufficient provision of basic necessities). While research in China has extensively documented associations between childhood trauma subtypes and adult substance use (*7*), investigations focusing on adolescent and young adult populations remain limited. This comprehensive cross-sectional study, encompassing 63 universities in Jilin Province, employed logistic regression analyses to evaluate the impact of various childhood trauma types on substance use patterns while controlling for relevant confounding variables. Our findings demonstrate that participants who experienced severe emotional abuse, sexual abuse, or physical neglect during childhood exhibited significantly elevated risks of substance use. Moreover, we observed a dose-response relationship between cumulative trauma exposure and substance use likelihood, highlighting the critical need for trauma-informed interventions and targeted support strategies for this vulnerable population.

This cross-sectional study employed cluster sampling through an online survey conducted from October 26th to November 18th, 2021, encompassing 63 universities and colleges in Jilin Province, China. Student participants represented various provinces across China. Data collection utilized a Quick Response (QR) code distributed to all participants, with online informed consent obtained prior to questionnaire completion. Study inclusion criteria comprised: 1) age above 15 years; 2) correct responses to at least three of four attention check questions; 3) physiologically plausible height and weight values; 4) absence of logical contradictions, missing answers, or irrelevant responses; and 5) no apparent pattern-based responding. After the screening, 96,151 participants qualified for analysis (male=40,039, 41.64%; mean age=19.59). The study received approval from the Jilin University ethics committee (No: 20210929). Sociodemographic data, including gender, age, residence, per capita disposable income, ethnicity, and educational status, were collected and adjusted as

confounders in the logistic model. The Childhood Trauma Questionnaire (CTQ), a 28-item assessment tool, evaluated experiences of emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. Respondents rated each item on a 5-point Likert scale from "Never True" to "Very often true," enabling detailed assessment of trauma frequency (*8*). The CTQ demonstrated good internal consistency with a Cronbach's alpha of 0.73. Substance use assessment included current smoking status, with follow-up questions distinguishing between e-cigarettes and traditional cigarettes (*9–10*). Alcohol consumption was categorized binarily as users versus non-users. Statistical analyses were conducted using SAS software (version 9.4, SAS Institute Inc., Cary, NC, USA). Logistic regression analyses calculated adjusted odds ratios (a*OR*s) comparing substance use prevalence between individuals with varying levels and types of abuse experiences versus those without trauma exposure. All childhood trauma subtypes were simultaneously included in the regression model to account for their independent effects.

Table 1 presents the sociodemographic characteristics of the study population. Overall, 13.24% of participants reported using cigarettes and/or electronic cigarettes, while 59.64% reported alcohol consumption. Among substance users, 4.37% reported concurrent use of cigarettes and electronic cigarettes. Table 2 elucidates the differential impact of childhood trauma subtypes on various forms of substance use, including smoking, cigarette use, e-cigarette use, and alcohol consumption. Participants who experienced severe emotional abuse, sexual abuse, and physical neglect during childhood demonstrated significantly elevated risks of substance use, with adjusted odds ratios (*aORs*) of 1.22 [95% confidence interval (*CI*): 1.04, 1.42] for emotional abuse, 1.54 (95% *CI*: 1.32, 1.80) for sexual abuse, and 1.11 (95% *CI*: 1.04, 1.19) for physical neglect. Our analysis further reveals the complex relationship between cumulative childhood trauma experiences and substance use behaviors (Table 3). Using participants who reported no childhood trauma as the reference group, we observed a dose-response relationship between the number of trauma types experienced and substance use likelihood. For individuals reporting a single trauma experience, the odds were elevated for smoking (*aOR*=1.15, 95% *CI*: 1.09, 1.21), e-cigarette use (*aOR*=1.15, 95% *CI*: 1.06, 1.25), and alcohol consumption (*aOR*=1.20, 95% *CI*: 1.16, 1.24). This pattern intensified with increasing trauma exposure: two trauma experiences (smoking: *aOR*=1.25, 95% *CI*: 1.19, 1.32; e-cigarette use: *aOR*=1.32, 95% *CI*: 1.22, 1.43; alcohol use: *aOR*=1.23, 95% *CI*: 1.19, 1.27), three trauma experiences (smoking: *aOR*=1.52, 95% *CI*: 1.41, 1.64; e-cigarette use: *aOR*=1.82, 95% *CI*: 1.64, 2.02; alcohol use: *aOR*=1.50, 95% *CI*: 1.42, 1.58), four trauma experiences (smoking: *aOR*=1.60, 95% *CI*: 1.44, 1.78; e-cigarette use: *aOR*=1.90, 95% *CI*: 1.64, 2.20; alcohol use: *aOR*=1.69, 95% *CI*: 1.56, 1.83), and five trauma experiences (smoking: *aOR*=1.82, 95% *CI*: 1.62, 2.05; e-cigarette use: *aOR*=2.48, 95% *CI*: 2.12, 2.89; alcohol use: *aOR*=2.03, 95% *CI*: 1.82, 2.26).

DISCUSSION

Our study examines the complex relationship between childhood trauma and substance use behaviors among Chinese adolescents and young adults, providing critical insights that advance both research understanding and intervention strategies. The findings from our comprehensive analysis, particularly those presented in Table 2 and Table 3, expand current knowledge by revealing sophisticated patterns and associations across diverse forms of childhood trauma and substance use behaviors (*11*).

The influence of childhood trauma on substance use behaviors demonstrated in our results aligns with established research highlighting the persistent effects of adverse childhood experiences (*11–12*). Emotional abuse emerged as a robust predictor across all substance use categories, including smoking, cigarette use, e-cigarette use, and alcohol consumption. The progressive increase in odds ratios corresponding to emotional abuse severity emphasizes the necessity for interventions targeting multiple dimensions of emotional maltreatment. Similarly, the pronounced impact of severe physical abuse on all forms of substance use reinforces the enduring consequences of physical maltreatment (*13*). Physical neglect exhibited a notable graded association with substance use behaviors, while sexual abuse emerged as a particularly potent predictor, demonstrating a clear dose-response relationship across all substance use outcomes. Furthermore, the distinct patterns observed in the association between emotional neglect and various substance use forms underscore the complexity of this relationship, warranting deeper investigation into the underlying mechanisms.

The cumulative risk hypothesis provides a theoretical framework explaining our findings, positing that the combined effect of multiple risk factors

TABLE 1. Sample sociodemographic characteristics, childhood trauma and substance use of 96,151 participants.

Variables	All (*N*=96,151, 100%)		Women (*N*=56,112, 58.36%)		Men (*N*=40,039, 41.64%)	
	Mean/N	SD/%	Mean/N	SD/%	Mean/N	SD/%
Age						
Mean (SD)	19.59	1.74	19.56	1.70	19.64	1.81
Ethnicity						
Han ethnic group	86,050	89.49	49,817	88.78	36,233	90.49
Others	10,101	10.51	6,295	11.22	3,806	9.51
Education background						
Undergraduate	90,554	94.18	53,047	94.54	37,507	93.68
Master	5,375	5.59	2,938	5.24	2,437	6.09
Doctoral	222	0.23	127	0.23	95	0.24
Area type prior to university/college enrollment						
Urban	48,899	50.86	29,109	51.88	19,790	49.43
Rural	47,252	49.14	27,003	48.12	20,249	50.57
Per capita disposable income (CNY)						
< 6,000	28,601	29.75	17,327	30.88	11,274	28.16
6,000–13,999	31,195	32.44	18,521	33.01	12,674	31.65
14,000–22,999	16,051	16.69	9,304	16.58	6,747	16.85
23,000–35,999	9,404	9.78	5,409	9.64	3,995	9.98
36,000–70,000	6,483	6.74	3,459	6.16	3,024	7.55
> 70,000	4,417	4.59	2,092	3.73	2,325	5.81
Substance use						
Any substance use	58,473	60.81	27,702	49.37	30,771	76.85
Cigarette use						
No	83,416	86.76	53,970	96.18	29,446	73.54
Electronic cigarette	470	0.49	194	0.35	276	0.69
Conventional cigarette	8,059	8.38	886	1.58	7,173	17.92
Both	4,206	4.37	1,062	1.89	3,144	7.85
Alcohol use						
Non-drinker	38,803	40.36	28,609	50.99	10,194	25.46
≤1 time a month	43,623	45.37	22,849	40.72	20,774	51.88
2–4 times a month	10,844	11.28	3,721	6.63	7,123	17.79
2–4 times a week	1,867	1.94	627	1.12	1,240	3.10
≥4 times a week	1,014	1.05	306	0.55	708	1.77
Childhood trauma						
Never experienced childhood trauma	38,534	40.08	24,903	44.38	13,631	34.04
Any type of trauma	57,617	59.92	31,209	55.62	26,408	65.96
Emotional abuse	12,786	13.30	7,830	13.95	4,956	12.38
Physical abuse	6,457	6.72	2,970	5.29	3,487	8.71
Sexual abuse	13,864	14.42	6,836	12.18	7,028	17.55
Physical neglect	39,219	40.79	20,242	36.07	18,977	47.40
Emotional neglect	37,665	39.17	20,270	36.12	17,395	43.45

Abbreviation: SD=standard deviation; CNY=Chinese Yuan.

TABLE 2. Adjusted odds ratios of substance use among participants with childhood trauma experience.

Childhood trauma experience	Substance use Smoker *vs.* non-smoker			Cigarette use Smoker *vs.* non-smoker			E-cigarette use Smoker *vs.* non-smoker			Alcohol use Drinker *vs.* non-drinker		
	aOR	(95% *CI*)	*P*	*aOR*	(95% *CI*)	*P*	*aOR*	(95% *CI*)	*P*	*aOR*	(95% *CI*)	*P*
Ever experienced childhood trauma Emotional abuse												
None	1			1			1			1		
Mild	1.16	1.11–1.22	<0.001	1.09	1.01–1.17	0.019	1.23	1.12–1.36	<0.001	1.17	1.12–1.23	<0.001
Moderate	1.22	1.09–1.37	0.001	1.25	1.07–1.46	0.004	1.36	1.12–1.67	0.002	1.25	1.11–1.39	0.001
Severe	1.22	1.04–1.42	0.013	1.63	1.34–1.98	<0.001	1.73	1.36–2.21	<0.001	1.23	1.06–1.44	0.006
Physical abuse												
None	1			1			1			1		
Mild	1.10	1.02–1.20	0.018	1.08	0.97–1.20	0.170	1.17	1.01–1.35	0.038	1.11	1.03–1.21	0.010
Moderate	0.98	0.87–1.10	0.725	0.98	0.85–1.12	0.742	1.02	0.85–1.23	0.826	1.00	0.89–1.12	0.988
Severe	0.98	0.85–1.13	0.799	0.99	0.84–1.18	0.942	0.95	0.76–1.20	0.685	0.99	0.86–1.14	0.880
Sexual abuse												
None	1			1			1			1		
Mild	1.39	1.32–1.46	<0.001	1.25	1.17–1.33	<0.001	1.35	1.23–1.48	<0.001	1.39	1.32–1.46	<0.001
Moderate	1.50	1.39–1.62	<0.001	1.48	1.35–1.61	<0.001	1.57	1.38–1.77	<0.001	1.50	1.40–1.62	<0.001
Severe	1.54	1.32–1.80	<0.001	1.27	1.06–1.51	0.008	1.55	1.24–1.95	0.001	1.39	1.20–1.62	<0.001
Physical neglect												
None	1			1			1			1		
Mild	1.11	1.07–1.15	<0.001	1.18	1.12–1.25	<0.001	1.11	1.02–1.20	0.012	1.09	1.05–1.13	<0.001
Moderate	1.21	1.16–1.27	<0.001	1.26	1.18–1.35	<0.001	1.24	1.13–1.37	<0.001	1.21	1.15–1.26	<0.001
Severe	1.11	1.04–1.19	0.003	1.35	1.24–1.47	<0.001	1.26	1.11–1.43	0.001	1.03	0.97–1.10	0.320
Emotional neglect												
None	1			1			1			1		
Mild	1.10	1.06–1.14	<0.001	0.86	0.81–0.90	<0.001	0.90	0.83–0.97	0.009	1.10	1.06–1.14	<0.001
Moderate	1.08	1.01–1.14	0.020	0.92	0.85–1.00	0.061	0.98	0.87–1.11	0.718	1.07	1.01–1.14	0.020
Severe	0.96	0.90–1.02	0.173	1.07	0.98–1.16	0.141	1.23	1.09–1.39	0.001	0.91	0.86–0.97	0.004

Abbreviation: *aOR*=adjusted odds ratio; *CI*=confidence interval.
* Adjusted for age, gender, ethnicity group, place of residence, and per capita disposable income.

TABLE 3. Oddsratios of substance use among participants with cumulative childhood trauma.

Cumulative childhood trauma experiences	Frequency		Any substance use *vs.* no substance use			Smoker *vs.* non-smoker			E-cigarette use *vs.* non-e-cigarette use			Drinker *vs.* non-drinker		
	N	%	*aOR*	(95% *CI*)	*P*	*aOR*	(95% *CI*)	*P*	*aOR*	(95% *CI*)	*P*	*aOR*	(95% *CI*)	*P*
Never	38,534	40.08	1			1			1			1		
One	24,559	25.54	1.20	1.16–1.24	<0.001	1.15	1.09–1.21	<0.001	1.15	1.06–1.25	0.001	1.20	1.16–1.24	<0.001
Two	20,730	21.56	1.26	1.21–1.31	<0.001	1.25	1.19–1.32	<0.001	1.32	1.22–1.43	<0.001	1.23	1.19–1.27	<0.001
Three	7,294	7.59	1.55	1.46–1.64	<0.001	1.52	1.41–1.64	<0.001	1.82	1.64–2.02	<0.001	1.50	1.42–1.58	<0.001
Four	3,080	3.20	1.71	1.58–1.86	<0.001	1.60	1.44–1.78	<0.001	1.90	1.64–2.20	<0.001	1.69	1.56–1.83	<0.001
Five	1,954	2.03	2.16	1.94–2.41	<0.001	1.82	1.62–2.05	<0.001	2.48	2.12–2.89	<0.001	2.03	1.82–2.26	<0.001

Abbreviation: *aOR*=adjusted odds ratio; *CI*=confidence interval.
* Adjusted for age, gender, ethnicity group, place of residence, and per capita disposable income.

exceeds the sum of individual risk exposures (*14*). Our analysis, detailed in Table 3, reveals a clear dose-response relationship between the number of trauma experiences and substance use behaviors, demonstrating that exposure to multiple forms of childhood trauma significantly increases the likelihood

of substance use. From a neurobiological perspective, cumulative trauma exposure may induce structural and functional alterations in key brain regions responsible for stress regulation, particularly the amygdala and prefrontal cortex, leading to compromised emotional regulation capabilities and subsequently elevated substance use risk (*14*). The substantially increased odds of substance use among individuals with multiple trauma experiences underscore the critical importance of implementing targeted interventions and preventive strategies for this vulnerable population.

This study was subject to several limitations warrant consideration. The reliance on self-reported data introduces potential recall and social desirability biases, while the cross-sectional design precludes definitive causal inferences. Future research would benefit from longitudinal cohort studies that track participants over extended periods to elucidate the temporal relationship between trauma exposure and substance use patterns. Time-lagged analyses could further illuminate the dynamic progression from trauma exposure to subsequent substance use behaviors. Additionally, while our large sample size enhances statistical power and generalizability, it also presents methodological challenges. In samples of this magnitude, even minor differences can achieve statistical significance, necessitating careful interpretation of effect sizes alongside *P* values.

Our findings underscore childhood trauma as a significant predictor of substance use behaviors, emphasizing the necessity for multi-tiered intervention strategies. Healthcare providers should implement trauma-informed care protocols, recognizing the profound impact of childhood trauma on substance use patterns. Early identification and intervention are crucial, particularly in clinical settings where trauma histories may influence treatment outcomes (*15*). Mental health professionals must consider both psychological and somatic manifestations when evaluating and treating patients with trauma histories. From a policy perspective, priority should be given to developing comprehensive programs that prevent childhood trauma and mitigate its effects through family support initiatives, trauma education, and expanded mental health services. Implementation of evidence-based policies supporting early intervention and sustained support for trauma-affected individuals can significantly reduce substance use burden and enhance population health outcomes.

Conflict of interest: No conflicts of interest.

Funding: High-Level Public Health Talent Development Program, Beijing Municipal Health Commission.

doi: 10.46234/ccdcw2025.027

[#] Corresponding authors: Xiaoqian Zhang, xiaoqian1211@tsinghua.edu.cn; Yingjie Zhang, yingjiezhang@tsinghua.edu.cn.

[1] Department of Health Policy and Management, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA; [2] Institute for Hospital Management, Tsinghua University, Shenzhen City, Guangdong Province, China; [3] Vanke School of Public Health, Tsinghua University, Beijing, China; [4] Wulituo Hospital of Beijing Shijingshan District, Beijing, China; [5] Nuffield Department of Population Health, University of Oxford, Oxford, UK; [6] School of Public Health, The University of Hong Kong, Hong Kong Special Administrative Region, China; [7] Northeast Asian Research Center, Jilin University, Changchun City, Jilin Province, China; [8] Department of Population, Resources and Environment, Northeast Asian Studies College, Jilin University, Changchun City, Jilin Province, China; [9] China Center for Aging Studies and Social-Economic Development, Jilin University, Changchun City, Jilin Province, China; [10] Tsinghua University Hospital, Beijing, China.

[&] Joint first authors.

Submitted: July 26, 2024
Accepted: October 21, 2024
Issued: January 31, 2025

REFERENCES

1. Wang J, Deng XJ, Wang JJ, Wang XW, Xu L. Substance use, sexual behaviours, and suicidal ideation and attempts among adolescents: findings from the 2004 Guangzhou youth risk behaviour survey. Public Health 2009;123(2):116 – 21. https://doi.org/10.1016/j.puhe.2008.10.013.
2. Xie HY, Di XB, Liu SW, Zeng XY, Meng ZD, Xiao L. Tobacco use and cessation among college students—China, 2021. China CDC Wkly 2022;4(21):448 – 51. https://doi.org/10.46234/ccdcw2022.100.
3. Wang WYY, He ZA, Feng NN, Cai YY. Electronic cigarette use in China: awareness, prevalence and regulation. Tob Induc Dis 2019;17:30. https://doi.org/10.18332/tid/105393.
4. Dai LJ, Lu WY, Wang JJ, Zhang LL, Zhu JF. Social environment exposure to electronic cigarettes and its association with e-cigarette use among adolescents in Shanghai, China. Front Public Health 2022;10:1005323. https://doi.org/10.3389/fpubh.2022.1005323.
5. Mei SL, Gao TT, Li JM, Zhang Y, Chai JX, Wang LY, et al. Internet addiction in college students and its relationship with cigarette smoking and alcohol use in Northeast China. Asia Pac Psychiatry 2017;9(4):e12281. https://doi.org/10.1111/appy.12281.
6. Zhong YY, Hu QY, Chen JH, Li YT, Chen RM, Li Y, et al. The impact of childhood trauma on adolescent depressive symptoms: the chain mediating role of borderline personality traits and self-control. BMC Psychiatry 2024;24(1):377. https://doi.org/10.1186/s12888-024-05829-6.
7. Cao HJ, Liang Y, Li XM, Zhu L, Wu LL, Liu HY, et al. Childhood maltreatment and affective symptoms and severity of drug addiction among Chinese male drug users: variable-centered and person-centered approaches. J Aggress Maltreat Trauma 2021;30(8):1007 – 27. https://doi.org/10.1080/10926771.2020.1796874.
8. Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, et al. Development and validation of a brief screening version of the childhood trauma questionnaire. Child Abuse Negl 2003;27(2):169 –

90. https://doi.org/10.1016/S0145-2134(02)00541-0.
9. Huang CL, Lin HH, Wang HH. The psychometric properties of the Chinese version of the fagerstrom test for nicotine dependence. Addict Behav 2006;31(12):2324 – 7. https://doi.org/10.1016/j.addbeh.2006.02.024.
10. Fagerström KO. Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment. Addict Behav 1978;3(3-4):235 – 41. https://doi.org/10.1016/0306-4603(78)90024-2.
11. Zhang SJ, Lin XJ, Liu JB, Pan YL, Zeng X, Chen FL, et al. Prevalence of childhood trauma measured by the short form of the childhood trauma questionnaire in people with substance use disorder: a meta-analysis. Psychiatry Res 2020;294:113524. https://doi.org/10.1016/j.psychres.2020.113524.
12. Fuchshuber J, Unterrainer HF. Childhood trauma, personality, and substance use disorder: the development of a neuropsychoanalytic addiction model. Front Psychiatry 2020;11:531. https://doi.org/10.3389/fpsyt.2020.00531.
13. Ji K, Finkelhor D. A meta-analysis of child physical abuse prevalence in China. Child Abuse Negl 2015;43:61 – 72. https://doi.org/10.1016/j.chiabu.2014.11.011.
14. Evans GW, Li DP, Whipple SS. Cumulative risk and child development. Psychol Bull 2013;139(6):1342 – 96. https://doi.org/10.1037/a0031808.
15. Raja S, Hasnain M, Hoersch M, Gove-Yin S, Rajagopalan C. Trauma informed care in medicine: current knowledge and future research directions. Fam Community Health 2015;38(3):216 – 26. https://doi.org/10.1097/FCH.0000000000000071.

Preplanned Studies

Suicide Risk and Its Associations with Psychiatric Symptoms and Sleep Disturbances in Schizophrenia Inpatients — Henan, Hebei, and Shandong Provinces and Beijing Municipality, China, 2019–2022

Chaowei Li[1]; Yun Chen[1]; Lyufeng Zhang[2]; Hongle Zhang[3]; Shun Zhang[4]; Qianqian Chen[5]; Meihua Yang[2]; Na Liang[2]; Sifan Hu[1]; Zhaojun Ni[1]; Lin Lu[1]; Xinyu Sun[1,#]; Hongqiang Sun[1]

Summary

What is already known about this topic?

Suicide behaviors are prevalent among inpatients with schizophrenia. However, the relationships between psychiatric symptoms, sleep disturbances, and suicide risk remain poorly understood in these high-risk populations.

What is added by this report?

In a study of 672 schizophrenia inpatients across 9 hospitals in 4 Chinese provinces, the prevalence of suicide risk was 22.3% [95% confidence interval (*CI*): 19.3%, 25.6%]. The study identified significant associations between suicide risk and multiple clinical factors, including poor sleep quality, depressive symptoms, anxiety symptoms, and other psychiatric manifestations such as thinking disorder and activation.

What are the implications for public health practice?

Understanding the common sleep-related and psychiatric factors associated with suicide risk in hospitalized schizophrenia patients will enable clinicians and policymakers to better identify clinical risk indicators and enhance the quality of suicide prevention and treatment programs.

Schizophrenia represents a severe mental disorder with substantial global disease burden. According to the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019, more than 20 million people worldwide live with schizophrenia, with the condition accounting for 12.2% of disability-adjusted life years across all mental disorders (*1*). The disorder exhibits a strong association with suicide (*2*), with lifetime prevalence rates of 26.8% for suicide attempts and approximately 5% for suicide deaths among individuals with schizophrenia (*3*). Identifying patients at risk of suicide to enable targeted interventions remains a significant clinical challenge. While extensive research has examined suicide risk factors in schizophrenia patients, the relationships between psychiatric symptoms, sleep disturbances, and suicide risk remain poorly understood in hospitalized populations. Notably, hospitalized patients face particularly high suicide risk, with approximately one-third of suicide behaviors in schizophrenia patients occurring during hospitalization or within one week of discharge, and elevated risk persisting throughout the first post-discharge year (*2*). This underscores the critical importance of suicide risk assessment at admission. This study investigated suicide risk patterns in hospitalized schizophrenia patients and identified associated factors across comprehensive psychopathological dimensions, including multiple psychiatric symptom domains and sleep disturbances. The findings indicate higher suicide risk prevalence among schizophrenia inpatients experiencing psychiatric symptoms and sleep disturbances. These results suggest that systematic evaluation and intervention targeting these symptoms may help guide clinical practice and improve suicide risk management in this population.

This cross-sectional study employed convenience sampling to recruit schizophrenia inpatients from nine hospitals across Beijing Municipality and Henan, Hebei, and Shandong provinces in China from August 2019 to July 2022. The Ethics Committee of Peking University Sixth Hospital approved the protocol (No. 2019-18), and all participants provided written informed consent. Eligible participants met the International Classification of Diseases (tenth edition) diagnostic criteria for schizophrenia, confirmed by the Mini-International Neuropsychiatric Interview (M.I.N.I.). Inclusion criteria required participants to be 18 years or older, have at least primary education, and score 20 or higher on the Mini-Mental State

Examination (MMSE). Exclusion criteria encompassed severe cardiac, hepatic, nephritic, or respiratory dysfunction and other serious diseases. This study collected general demographic data and clinical characteristics. Psychiatric symptoms were evaluated using the Brief Psychiatric Rating Scale (BPRS), an 18-item scale ranging from 18 to 126 points, with higher scores indicating greater symptom severity. The BPRS comprises 5 factors: withdrawal-retardation, thinking disorder, anxious-depression, hostile-suspiciousness, and activation. Depressive and anxiety symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) self-rated scales, respectively. Sleep disturbances were evaluated using the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS), while cognitive performance was assessed using the Montreal Cognitive Assessment (MoCA). Suicide risk was categorized as none, mild, or moderate to severe based on scores from the M.I.N.I. (version 6.0) suicide module, administered by uniformly trained psychiatrists. The primary outcome was current suicide risk, defined as mild, moderate, or severe risk. Secondary outcomes included current suicidal ideation, suicide plan, and suicide attempt in the past month, as determined by specific questions in the M.I.N.I. suicide module. Of 714 invited inpatients, 672 participants (94.1% response rate) provided valid data and were included in the final analysis.

Measurement data of normal distribution were expressed as $\bar{x} \pm s$, and an independent sample *t*-test was used to compare the two groups. Non-normally distributed data were represented by M (Q_1, Q_3), and the Mann-Whitney *U* test was used to compare groups. Count data were expressed as *n* (%), and the χ^2 test was used for comparisons. A multivariable logistic regression was applied to obtain independent associated factors of suicide risk. All statistical methods used a two-tailed test, and differences where $P<0.05$ were considered statistically significant. All statistical analyses were performed using SPSS software (version 25.0. IBM Corp., Armonk, NY, USA).

Among the hospitalized patients with schizophrenia, the median age was 38 years, with females comprising 33.0% (222/672) of the cohort. All patients were receiving antipsychotic medication. The prevalence of PHQ-9-defined depressive symptoms and GAD-7-defined anxiety symptoms was 12.4% (83/672) and 7.9% (53/672), respectively. Sleep disturbances were common, with 56.8% (382/672) of patients experiencing poor sleep quality (PSQI score >5) and 19.2% (129/672) reporting daytime sleepiness (ESS score >10). Mild cognitive impairment (MCI) was present in 77.8% (523/672) of patients, as defined by a MoCA score below 26.

The overall prevalence of suicide risk in hospitalized patients with schizophrenia was 22.3% [95% confidence interval (*CI*): 19.3%, 25.6%], with 14.6% (98/672) classified as mild risk and 7.8% (52/672) as moderate to severe risk. Current suicidal ideation was present in 10.9% (73/672) of patients, while 2.5% (17/672) reported suicide plans and 3.3% (22/672) had attempted suicide.

Analysis of demographic and clinical characteristics revealed that patients with suicide risk were significantly younger than those without risk (median age 35 years *vs.* 39 years, $P=0.004$). Age stratification showed a higher proportion of younger patients (18–35 years) in the suicide risk group (53.3% *vs.* 41.4%, $P=0.010$). Additionally, patients with suicide risk had a higher rate of previous modified electroconvulsive therapy (35.3% *vs.* 23.8%, $P=0.005$). No significant differences were observed between groups regarding sex distribution, education level, body mass index (BMI), or marital status (Table 1).

Regarding psychiatric symptoms and sleep disturbances, patients with suicide risk exhibited significantly higher rates of poor sleep quality (73.3% *vs.* 52.1%, $P<0.001$), daytime sleepiness (25.3% *vs.* 17.4%, $P=0.030$), depressive symptoms (32.7% *vs.* 6.5%, $P<0.001$), and anxiety symptoms (26.0% *vs.* 2.7%, $P<0.001$) compared to those without suicide risk. Total BPRS scores, factor scores (anxious-depression and activation), PHQ-9, GAD-7, PSQI, and ESS scores were also significantly elevated (all $P<0.01$), while the thinking disorder factor score was lower ($P=0.036$) (Table 1). Among patients with varying levels of suicide risk, BPRS total scores, PHQ-9, GAD-7, and PSQI scores showed positive correlations (Figure 1A), and the prevalence of depressive symptoms, anxiety symptoms, and poor sleep quality increased proportionally with suicide risk level (Figure 1B). Neither the level nor the prevalence of daytime sleepiness showed significant increases with elevated suicide risk.

In the multivariable logistic regression analysis, multiple potential contributors to suicide risk were considered including: sex, age group, marital status, education, BMI, disease duration, family history of mental disorders, history of drug allergy, histories of smoking and alcohol consumption, modified electroconvulsive therapy history, MCI, anxiety

TABLE 1. Demographic characteristics, clinical characteristics, sleep parameters and psychiatric symptoms of schizophrenia inpatients with and without suicide risk.

Variable	Total (*N*=672)	Schizophrenia with suicide risk (*N*=150)	Schizophrenia without suicide risk (*N*=522)	χ^2/Z-value	*P*
Demographic characteristics					
Sex [*n* (%)]				0.253	0.615
Male	450 (67.0)	103 (68.7)	347 (66.5)		
Female	222 (33.0)	47 (31.3)	175 (33.5)		
Age [years, M (Q1, Q3)]	38.00 (30.00, 49.00)	35.00 (27.00, 45.00)	39.00 (30.00, 49.00)	−2.899	0.004
Age group (years)				9.184	0.010
18–35 [*n* (%)]	296 (44.0)	80 (53.3)	216 (41.4)		
36–60 [*n* (%)]	340 (50.6)	67 (44.7)	273 (52.3)		
>60 [*n* (%)]	36 (5.4)	3 (2.0)	33 (6.3)		
Marital status [*n* (%)]				1.112	0.292
Married	192 (28.6)	48 (32.0)	144 (27.6)		
Not married	480 (71.4)	102 (68.0)	378 (72.4)		
Education [*n* (%)]				0.934	0.334
College or above	121 (18.0)	23 (15.3)	98 (18.8)		
Lower than college	551 (82.0)	127 (84.7)	424 (81.2)		
BMI [kg/m^2, M (Q1, Q3)]	24.77 (22.08, 27.69)	24.60 (21.88, 27.69)	24.82 (22.18, 27.70)	−0.229	0.819
Clinical characteristics					
Disease duration [years, M (Q1, Q3)]	11.00 (5.00, 20.00)	10.00 (5.00, 16.00)	11.00 (5.00, 20.00)	−1.698	0.089
Family history of mental disorders [*n* (%)]				0.489	0.485
Yes	97 (14.4)	19 (12.7)	78 (14.9)		
No	575 (85.6)	131 (87.3)	444 (85.1)		
History of drug allergy [*n* (%)]				0.195	0.659
Yes	23 (3.4)	6 (4.0)	17 (3.3)		
No	649 (96.6)	144 (96.0)	505 (96.7)		
History of alcohol consumption [*n* (%)]				2.541	0.111
Yes	40 (6.0)	13 (8.7)	27 (5.2)		
No	632 (94.0)	137 (91.3)	495 (94.8)		
History of smoking [*n* (%)]				2.350	0.125
Yes	161 (24.0)	43 (28.7)	118 (22.6)		
No	511 (76.0)	107 (71.3)	404 (77.4)		
MECT history [*n* (%)]				8.051	0.005
Yes	177 (26.3)	53 (35.3)	124 (23.8)		
No	495 (73.7)	97 (64.7)	398 (76.2)		
Current medication					
Antipsychotics [*n* (%)]	672 (100)	150 (100)	522 (100)	NA	NA
Antidepressants [*n* (%)]	54 (8.0)	15 (10.0)	39 (7.5)	1.008	0.315
Sedative-hypnotics [*n* (%)]	195 (29.0)	42 (28.0)	153 (29.3)	0.097	0.755
Mood stabilizers [*n* (%)]	109 (16.2)	22 (14.7)	87 (16.7)	0.343	0.558
Sleep parameters					
PSQI [M (Q1, Q3)]					
Subjective sleep quality	1.00 (0, 1.00)	1.00 (1.00, 2.00)	1.00 (0, 1.00)	−5.329	<0.001

Continued

Variable	Total (*N*=672)	Schizophrenia with suicide risk (*N*=150)	Schizophrenia without suicide risk (*N*=522)	χ^2/Z-value	*P*
Sleep latency	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	1.00 (0, 2.00)	−2.071	0.038
Sleep duration	0 (0, 1.00)	0 (0, 1.00)	0 (0, 1.00)	−3.224	0.001
Habitual sleep efficiency	0 (0, 1.00)	0 (0, 2.00)	0 (0, 1.00)	−2.395	0.017
Sleep disturbances	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.00 (0, 1.00)	−4.513	<0.001
Use of sleeping medication	1.00 (0, 3.00)	2.00 (0, 3.00)	1.00 (0, 3.00)	−2.618	0.009
Daytime dysfunction	1.00 (0, 2.00)	2.00 (1.00, 3.00)	1.00 (0, 2.00)	−6.243	<0.001
Total score	6.00 (3.00, 10.00)	8.50 (5.00, 11.00)	6.00 (3.00, 9.00)	−5.656	<0.001
Poor sleep quality [*n* (%)]				21.400	<0.001
Yes	382 (56.8)	110 (73.3)	272 (52.1)		
No	290 (43.2)	40 (26.7)	250 (47.9)		
ESS total score [M (Q1, Q3)]	5.00 (1.00, 9.00)	6.00 (2.00, 11.00)	5.00 (0, 9.00)	−3.094	0.002
Daytime sleepiness [*n* (%)]				4.689	0.030
Yes	129 (19.2)	38 (25.3)	91 (17.4)		
No	543 (80.8)	112 (74.7)	431 (82.6)		
Psychiatric symptoms					
MoCA total score [M (Q1, Q3)]	22.00 (18.00, 25.00)	22.00 (18.00, 25.00)	22.00 (18.00, 25.00)	−0.847	0.397
Mild cognitive impairment [*n* (%)]				1.375	0.241
Yes	523 (77.8)	122 (81.3)	401 (76.8)		
No	149 (22.2)	28 (18.7)	121 (23.2)		
PHQ-9 total score [M (Q1, Q3)]	3.00 (0, 7.00)	8.00 (4.00, 12.00)	2.00 (0, 4.00)	−11.399	<0.001
Depressive symptom [*n* (%)]				73.619	<0.001
Yes	83 (12.4)	49 (32.7)	34 (6.5)		
No	589 (87.6)	101 (67.3)	488 (93.5)		
GAD-7 total score [M (Q1, Q3)]	1.00 (0, 4.75)	5.50 (1.00, 10.00)	0.50 (0, 3.00)	−9.951	<0.001
Anxiety symptom [n (%)]				87.206	<0.001
Yes	53 (7.9)	39 (26.0)	14 (2.7)		
No	619 (92.1)	111 (74.0)	508 (97.3)		
BPRS [M (Q1, Q3)]					
Withdrawal-retardation	2.00 (1.50, 2.50)	2.00 (1.50, 2.50)	2.25 (1.50, 2.50)	−0.457	0.648
Thinking disorder	1.50 (1.00, 2.25)	1.50 (1.00, 2.25)	1.75 (1.00, 2.50)	−2.093	0.036
Anxious-depression	1.75 (1.00, 2.50)	2.50 (2.00, 3.00)	1.50 (1.00, 2.06)	−9.502	<0.001
Hostile-suspiciousness	2.00 (1.00, 2.67)	2.33 (1.00, 2.67)	2.00 (1.00, 2.67)	−1.010	0.313
Activation	1.00 (1.00, 1.67)	1.67 (1.00, 1.67)	1.00 (1.00, 1.67)	−5.155	<0.001
Total score	33.00 (27.00, 38.00)	35.00 (30.00, 40.00)	32.00 (27.00, 38.00)	−3.824	<0.001

Note: Poor sleep quality is defined as PSQI >5. Daytime sleepiness is defined as ESS >10. MCI is defined as MoCA <26. Depressive symptom is defined as PHQ-9 ≥10. Anxiety symptom is defined as GAD-7 ≥10. Continuous variables not conforming to the normal distribution were expressed as M (Q1, Q3); categorical variables were expressed as *n* (%).

Abbreviation: M=median; Q1=lower quartile; Q3=upper quartile; BMI=body mass index; MECT=modified electroconvulsive therapy; PSQI=Pittsburgh Sleep Quality Index; ESS=Epworth Sleepiness Scale; MoCA=Montreal Cognitive Assessment; BPRS=Brief Psychiatric Rating Scale; PHQ-9=Patient Health Questionnaire-9; GAD-7=Generalized Anxiety Disorder-7.

symptoms, depressive symptoms, poor sleep quality, daytime sleepiness, and BPRS factor scores (withdrawal-retardation, thinking disorder, hostile-suspiciousness, and activation). The anxious-depression factor of BPRS was excluded due to the presence of PHQ-9-defined depressive symptoms and GAD-7-defined anxiety symptoms. The analysis revealed that suicide risk in schizophrenia was independently

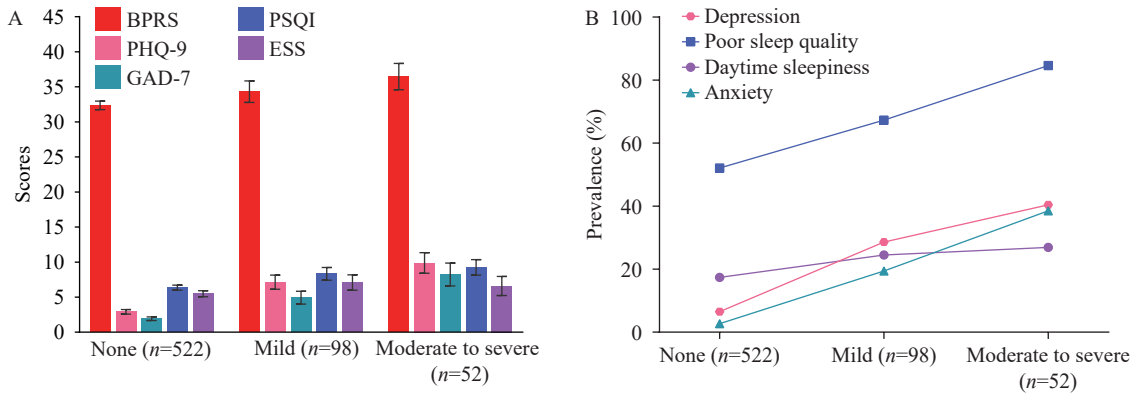


FIGURE 1. Psychiatric symptoms and sleep disturbances in schizophrenia inpatients with different suicide risk levels. (A) Scores; (B) Prevalence.
Note: Error bars indicate 95% *CI*s. Suicide risk was categorized as none, mild, or moderate to severe according to the Mini-International Neuropsychiatric Interview suicide module assessment by trained psychiatrists. Anxiety is defined as GAD-7≥ 10. Depression is defined as PHQ-9≥10. Poor sleep quality is defined as PSQI>5. Daytime sleepiness is defined as ESS>10.
Abbreviation: BPRS=Brief Psychiatric Rating Scale; PHQ-9=Patient Health Questionnaire-9; GAD-7=Generalized Anxiety Disorder-7; PSQI=Pittsburgh Sleep Quality Index; ESS=Epworth Sleepiness Scale; *CI*=confidence interval.

associated with poor sleep quality [adjusted odds ratio (*aOR*)=2.09, 95% *CI*: 1.31, 3.36, *P*=0.002], depressive symptoms (*aOR*=2.24, 95% *CI*: 1.19, 4.23, *P*=0.013), anxiety symptoms (*aOR*=6.91, 95% *CI*: 3.10, 15.41, *P*<0.001), thinking disorder (*aOR*=0.55, 95% *CI*: 0.39, 0.80, *P*=0.002), and activation (*aOR*=1.85, 95% *CI*: 1.13, 3.04, *P*=0.014) (Table 2).

DISCUSSION

These findings demonstrate a high prevalence of suicide risk among hospitalized patients with schizophrenia, with significant associations between suicide risk and both psychiatric symptoms and sleep disturbances. The results indicate that schizophrenia inpatients with suicide risk are characterized by younger age, lower levels of thinking disorder, and higher levels of activation, coupled with anxiety symptoms, depressive symptoms, and poor sleep quality compared to those without suicide risk. These findings suggest that systematic evaluation and targeted intervention for these symptoms may help reduce suicide risk in clinical settings and improve both clinical practice and health management strategies.

Previous studies of schizophrenia patients in China have reported suicidal ideation prevalence rates ranging from 7.4% to 57.6% (*4*). Meta-analytic evidence indicates lifetime and point prevalence rates of suicidal ideation among schizophrenia patients of 34.5% and 29.9%, respectively, while lifetime and point prevalence rates of suicide plans were 44.3% and 6.4%–13%, respectively (*5*). The 1-month prevalence of suicide attempts in patients with schizophrenia was reported at 2.7% across studies (*6*). In this study, the prevalence of suicide risk (22.3%, 95% *CI*: 19.3%, 25.6%) was lower than anticipated, potentially due to the sample characteristics. Since this cohort consisted of hospitalized patients with extended disease duration, their psychiatric symptoms and sleep disorders were relatively mild post-treatment compared to those in acute episodes.

The relationship between psychiatric symptoms and suicide risk in schizophrenia patients has been extensively investigated. While some studies suggest that increased positive symptoms, such as hallucinations and delusions, are associated with suicide (*7*–*8*), evidence indicates that command auditory hallucinations specifically, rather than auditory hallucinations in general, correlate with suicidal behavior (*8*). The nature of psychotic symptoms is highly complex and variable, with marked individual differences. The elevated suicide risk may stem not from the psychotic symptoms themselves but from the accompanying distress, depression, and hopelessness (*9*). Suicide rates were notably higher among schizophrenia patients experiencing depression and anxiety, particularly depressed mood and hopelessness (*2*). This study reveals that suicide risk in schizophrenia inpatients is associated with multiple psychiatric symptoms: anxiety, depression, thinking disorder, and activation. These results underscore the critical importance of comprehensive assessment of

TABLE 2. Unadjusted and adjusted *OR*s of associated factors of suicide risk in schizophrenia inpatients.

Variable	Unadjusted *OR* (95% *CI*)	*P*	Adjusted *OR* (95% *CI*)*	*P*
Sex				
Male	1	–	1	–
Female	0.91 (0.61, 1.34)	0.615	0.90 (0.54, 1.51)	0.680
Age group (years)				
18–35	1	–	1	–
36–60	0.66 (0.46, 0.96)	0.029	0.80 (0.48, 1.33)	0.386
>60	0.25 (0.07, 0.82)	0.023	0.36 (0.09, 1.55)	0.171
Marital status				
Not married	1	–	1	–
Married	1.24 (0.83, 1.83)	0.292	1.44 (0.89, 2.35)	0.141
Education				
Lower than college	1	–	1	–
College or above	0.78 (0.48, 1.29)	0.335	1.02 (0.57, 1.80)	0.954
BMI (kg/m^2)	1.00 (0.96, 1.04)	0.922	0.99 (0.94, 1.03)	0.518
Disease duration (years)	0.98 (0.96, 1.00)	0.030	1.00 (0.97, 1.02)	0.725
Family history of mental disorders				
No	1	–	1	–
Yes	0.83 (0.48, 1.41)	0.485	1.05 (0.56, 1.98)	0.873
History of drug allergy				
No	1	–	1	–
Yes	1.24 (0.48, 3.20)	0.660	0.63 (0.18, 2.22)	0.472
History of alcohol consumption				
No	1	–	1	–
Yes	1.74 (0.87, 3.46)	0.115	1.18 (0.49, 2.89)	0.712
History of smoking				
No	1	–	1	–
Yes	1.38 (0.91, 2.07)	0.126	1.22 (0.71, 2.10)	0.481
MECT history				
No	1	–	1	–
Yes	1.75 (1.19, 2.59)	0.005	1.36 (0.84, 2.20)	0.209
Poor sleep quality				
No	1	–	1	–
Yes	2.53 (1.69, 3.77)	<0.001	2.09 (1.31, 3.36)	0.002
Daytime sleepiness				
No	1	–	1	–
Yes	1.61 (1.04, 2.48)	0.031	1.02 (0.60, 1.72)	0.950
Mild cognitive impairment				
No	1	–	1	–
Yes	1.32 (0.83, 2.08)	0.242	1.23 (0.72, 2.10)	0.454
Depressive symptom				
No	1	–	1	–
Yes	6.96 (4.28, 11.33)	<0.001	2.24 (1.19, 4.23)	0.013

Continued

Variable	Unadjusted *OR* (95% *CI*)	*P*	Adjusted *OR* (95% *CI*)*	*P*
Anxiety symptom				
No	1	–	1	–
Yes	12.75 (6.69, 24.28)	<0.001	6.91 (3.10, 15.41)	<0.001
Withdrawal-retardation	0.94 (0.72, 1.22)	0.637	0.73 (0.52, 1.03)	0.070
Thinking disorder	0.73 (0.56, 0.94)	0.013	0.55 (0.39, 0.80)	0.002
Hostile-suspiciousness	1.06 (0.88, 1.29)	0.524	1.09 (0.82, 1.45)	0.537
Activation	2.46 (1.67, 3.63)	<0.001	1.85 (1.13, 3.04)	0.014

Abbreviation: *OR*=odds ratio; *CI*=confidence interval; BMI=body mass index; MECT=modified electroconvulsive therapy.
* *OR* was adjusted for the variables listed above in a multivariable logistic regression model.

both affective and positive symptoms in schizophrenia patients for timely identification of suicide risk.

Sleep disturbances are highly prevalent in schizophrenia, affecting up to 80% of patients, with manifestations including difficulties in initiating or maintaining sleep and excessive daytime sleepiness (*10*). Among these disturbances, insomnia represents the predominant sleep disorder in schizophrenia patients, occurring at significantly higher rates compared to the general population (*11*). This study demonstrates that both the prevalence and severity of poor sleep quality increased proportionally with suicide risk level, providing further evidence for the robust association between sleep disturbances and suicide risk in schizophrenia.

This investigation has three primary limitations. First, the cross-sectional study design only allows for the identification of correlative factors associated with suicide risk and cannot establish causality; additionally, recall bias remains an inherent challenge. Second, while the M.I.N.I. effectively assesses current suicide risk, it cannot predict progression to death by suicide. Third, the relatively small sample size constrains the study's statistical power and generalizability, necessitating larger-scale investigations to validate these findings.

In conclusion, this study emphasizes the critical importance of suicide risk assessment in schizophrenia inpatients. Comprehensive monitoring of psychiatric symptoms and sleep disturbances can facilitate early identification of patients at elevated suicide risk, and timely intervention targeting these symptoms may help reduce suicide risk. When clinicians identify these symptoms in hospitalized schizophrenia patients, they should alert family members and community healthcare providers to maintain vigilant suicide prevention measures following discharge.

Conflicts of interest: No conflicts of interest.

Acknowledgements: The project teams from Peking University Sixth Hospital, Beijing Changping District Hospital of Integrated Traditional Chinese and Western Medicine, Beijing Tongzhou Psychiatric Hospital, Beijing Chaoyang Third Hospital, Beijing Xicheng District Ping'an Hospital, Zhumadian Second People's Hospital, Liaocheng Fourth People's Hospital, Fifth Hospital of Qinhuangdao, and Kailuan Mental Health Centre, and all study participants. Yanping Bao for providing valuable guidance on statistical analysis.

Funding: Supported by the Ministry of Science and Technology of the People's Republic of China (STI2030-Major Projects2021ZD0201900) and the National Natural Science Foundation of China (81971235).

doi: 10.46234/ccdcw2025.028

[#] Corresponding author: Xinyu Sun, sunxinyu@bjmu.edu.cn.

[1] Peking University Sixth Hospital, Peking University Institute of Mental Health, NHC Key Laboratory of Mental Health (Peking University), National Clinical Research Center for Mental Disorders (Peking University Sixth Hospital), Beijing, China; [2] Zhumadian Second People's Hospital, Zhumadian Psychiatric Hospital, Zhumadian City, Henan Province, China; [3] Liaocheng Fourth People's Hospital, Liaocheng City, Shandong Province, China; [4] Kailuan Mental Health Centre, Tangshan City, Hebei Province, China; [5] Fifth Hospital of Qinhuangdao, Qinhuangdao City, Hebei Province, China.

Submitted: July 09, 2024
Accepted: January 09, 2025
Issued: January 31, 2025

REFERENCES

1. GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry 2022;9(2):137 – 50. https://doi.org/10.1016/S2215-0366(21)00395-3.
2. Popovic D, Benabarre A, Crespo JM, Goikolea JM, González-Pinto A,

Gutiérrez-Rojas L, et al. Risk factors for suicide in schizophrenia: systematic review and clinical recommendations. Acta Psychiatr Scand 2014;130(6):418 – 26. https://doi.org/10.1111/acps.12332.
3. Hor K, Taylor M. Suicide and schizophrenia: a systematic review of rates and risk factors. J Psychopharmacol 2010;24(S4):81 – 90. https://doi.org/10.1177/1359786810385490.
4. Dong M, Wang SB, Wang F, Zhang L, Ungvari GS, Ng CH, et al. Suicide-related behaviours in schizophrenia in China: a comprehensive meta-analysis. Epidemiol Psychiatr Sci 2019;28(3):290 – 9. https://doi.org/10.1017/S2045796017000476.
5. Bai W, Liu ZH, Jiang YY, Zhang QE, Rao WW, Cheung T, et al. Worldwide prevalence of suicidal ideation and suicide plan among people with schizophrenia: a meta-analysis and systematic review of epidemiological surveys. Transl Psychiatry 2021;11(1):552. https://doi.org/10.1038/s41398-021-01671-6.
6. Lu L, Dong M, Zhang L, Zhu XM, Ungvari GS, Ng CH, et al. Prevalence of suicide attempts in individuals with schizophrenia: a meta-analysis of observational studies. Epidemiol Psychiatr Sci 2019;29:e39. https://doi.org/10.1017/S2045796019000313.
7. Fenton WS. Depression, suicide, and suicide prevention in schizophrenia. Suicide Life Threat Behav 2000;30(1):34 – 49. https://doi.org/10.1111/j.1943-278X.2000.tb01063.x.
8. Wong Z, Öngür D, Cohen B, Ravichandran C, Noam G, Murphy B. Command hallucinations and clinical characteristics of suicidality in patients with psychotic spectrum disorders. Compr Psychiatry 2013;54(6):611 – 7. https://doi.org/10.1016/j.comppsych.2012.12.022.
9. Hettige NC, Bani-Fatemi A, Sakinofsky I, De Luca V. A biopsychosocial evaluation of the risk for suicide in schizophrenia. CNS Spectr 2018;23(4):253 – 63. https://doi.org/10.1017/S1092852917000128.
10. Cohrs S. Sleep disturbances in patients with schizophrenia: impact and effect of antipsychotics. CNS Drugs 2008;22(11):939 – 62. https://doi.org/10.2165/00023210-200822110-00004.
11. Laskemoen JF, Simonsen C, Büchmann C, Barrett EA, Bjella T, Lagerberg TV, et al. Sleep disturbances in schizophrenia spectrum and bipolar disorders - a transdiagnostic perspective. Compr Psychiatry 2019;91:6 – 12. https://doi.org/10.1016/j.comppsych.2019.02.006.

Preplanned Studies

Temporal Trends in Cardiovascular Disease Mortality Attributable to Ambient Particulate Matter Pollution — China, 1990–2021

Yunning Liu[1]; Wu Yan[2]; Lijun Wang[1]; Jing Wu[1,#]

Summary

What is already known about this topic?

Cardiovascular disease (CVD) represents a major cause of mortality and disability in China's population. Ambient particulate matter pollution (APMP) has been established as a significant risk factor contributing to CVD development.

What is added by this report?

Analysis of data from 1990 to 2021 reveals a substantial increase in APMP-attributable CVD mortality across China. While recent trends show decreased mortality risk associated with APMP-attributable CVD, birth cohort analysis demonstrates continued risk elevation in males but declining risk in females born after 1971.

What are the implications for public health practice?

Enhanced surveillance and regulation of APMP, coupled with targeted health promotion strategies, are crucial, particularly for elderly populations and males who show increased vulnerability.

Cardiovascular disease (CVD) is a leading cause of death and disability in China. This study aims to assess the long-term trends of ambient particulate matter pollution (APMP) attributable CVD mortality in China. Data were extracted from Global Burden of Disease 2021 and an age-period-cohort was used. From 1990 to 2021, APMP-attributable CVD mortality increased by 101.6% in China (increased by 101.8% in males and 100.0% in females). The mortality risk associated with APMP-attributable CVD decreased recently for both males and females (after 2017). In different birth cohort, the mortality risk continued to increase in males but decreased in females born after 1971. More effective efforts are needed to mitigate the increasing trends of APMP-attributable CVD mortality, especially for males.

CVD represents a substantial public health burden in China, contributing significantly to mortality and disability while imposing considerable strain on the healthcare system through rapidly escalating costs (*1*). By 2020, CVD accounted for approximately two-fifths of all deaths in China (*2*). APMP has emerged as a critical risk factor for CVD development. Chronic exposure to APMP has been associated with increased risk of various cardiovascular conditions, including atherosclerosis, hypertension, coronary heart disease, and stroke (*3*).

Understanding the CVD burden attributable to APMP exposure in the Chinese population is crucial for developing evidence-based prevention strategies. This study characterizes the longitudinal trends of APMP's impact on CVD mortality and examines the underlying factors driving these patterns. Our findings provide valuable insights into the health burden of APMP-attributable CVD in China, which may inform future public health interventions and policy decisions.

Data on APMP-attributable CVD mortality were obtained from the Global Burden of Disease (GBD) 2021 database (*4*–*5*). APMP measurements integrated multiple data sources, including ground monitoring stations, satellite aerosol observations, chemical transport modeling, population estimates, and land-use data. APMP was defined as the population-weighted annual average daily exposure to outdoor particulate matter with an aerodynamic diameter less than 2.5 μg per cubic meter of air (*4*). APMP-attributable CVD mortality was calculated using exposure levels compared against a theoretical minimum risk exposure level counterfactual scenario. The exposure-response relationships were derived from cohort studies, pooled cohort analyses, and randomized controlled trials. Population data were sourced from the 2022 Revision of World Population Prospects (WPP), which incorporated national censuses, vital registration systems, and representative population surveys.

An age-period-cohort (APC) analysis was conducted to elucidate the underlying effects driving long-term trends in APMP-attributable CVD mortality. The analysis utilized mortality and population data categorized into consecutive 5-year periods (1992–2021) and 5-year age intervals (25–89 years).

Data from 1990–1991 were excluded due to insufficient data for complete 5-year periods. The following parameters were estimated: net drift (overall annual percentage change), local drift (age-specific annual percentage changes), longitudinal age curve (age-specific mortality risk), period relative risk (RR) (temporal variations in mortality risk), and cohort RR (birth cohort-specific mortality risk). Parameter estimation was performed using the National Cancer Institute's R program (*6*). Statistical significance of estimable parameters and functions was assessed using Wald chi-square tests. Analyses were conducted using R (version 4.2.1; R Foundation for Statistical Computing, Vienna, Austria) 4.2.1, with statistical significance set at $P<0.05$.

Figure 1 illustrates the temporal trends in age-standardized APMP-attributable CVD mortality. In 2021, the age-standardized mortality rate per 100,000 population was 66.4 [95% uncertainty interval (*UI*): 44.9, 84.2] for both sexes combined, with rates of 90.7 (95% *UI*: 61.1, 116.0) for males and 49.9 (95% *UI*: 30.9, 65.9) for females. Between 1990 and 2021, the age-standardized mortality rate increased by 101.6% overall, with similar increases observed in both males (101.8%) and females (100.0%). The mortality rate peaked in 2014 at 82.1 (95% *UI*: 52.2, 102.9) per 100,000 population, followed by a declining trend that was interrupted in 2021.

The net drift, representing the annual percentage change in expected age-adjusted rates over time, was 2.3% [95% confidence interval (*CI*): 2.1%, 2.5%] for APMP-attributable CVD mortality, with males showing 2.4% (95% *CI*: 2.2%, 2.6%) and females showing 1.1% (95% *CI*: 0.6%, 1.7%) (Figure 2).

Local drift analysis, which measures the annual percentage change in expected age-specific rates over time, revealed significant positive values ($P<0.05$) for both males and females aged over 55 years. Peak local drift values were observed at 3.6% (95% *CI*: 2.2%, 4.9%) in males aged 25–29 years and 4.1% (95% *CI*: 3.2%, 4.9%) in females aged 85–89 years.

The longitudinal age curve, representing the age effect, demonstrates that APMP-attributable CVD mortality increased dramatically with age, rising from 0.7 per 100,000 population in the 25–29-year age group to 3,470.0 in the 85–89 age group. This pattern of exponential increase with age was consistent across both males and females (Figure 3A).

The period and cohort effects, expressed as relative risk (*RR*), represent the ratio of age-specific rates in each period or cohort relative to their respective reference groups. Period *RR*s showed an upward trend for both males and females until 2017, followed by a decline in mortality risk during the most recent period (2017–2021) (Figure 3B). The cohort effect analysis revealed divergent patterns between genders: males demonstrated a continuous increase in *RR* across successive birth cohorts, while females showed a decreasing trend in mortality risk for cohorts born after 1971 (Figure 3C).

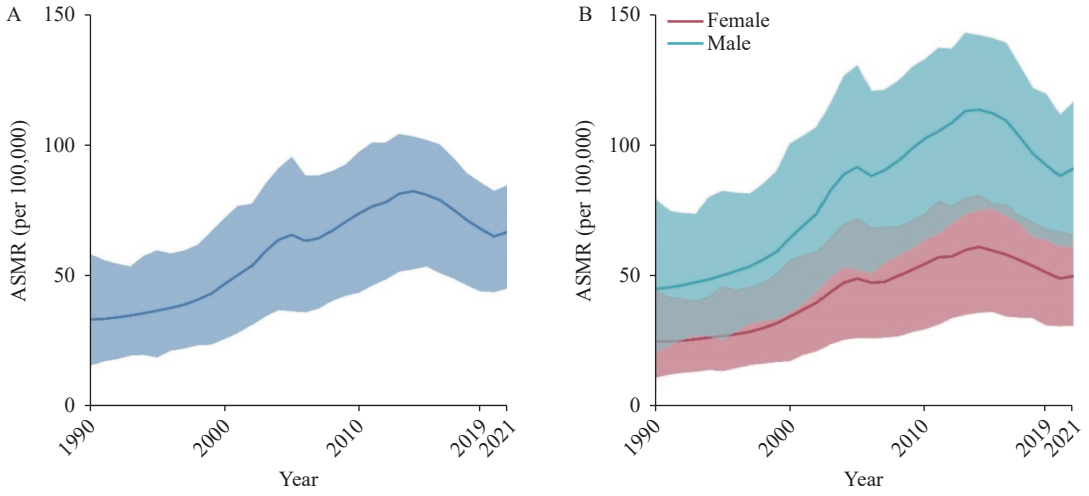


FIGURE 1. Temporal trends in age-standardized APMP-attributable CVD mortality in China, 1990–2021. (A) Combined trends for both sexes; (B) Sex-specific trends for males and females.
Note: Shaded areas represent 95% uncertainty intervals.
Abbreviation: ASMR=age-standardized mortality rate; APMP=ambient particulate matter pollution; CVD=cardiovascular disease.

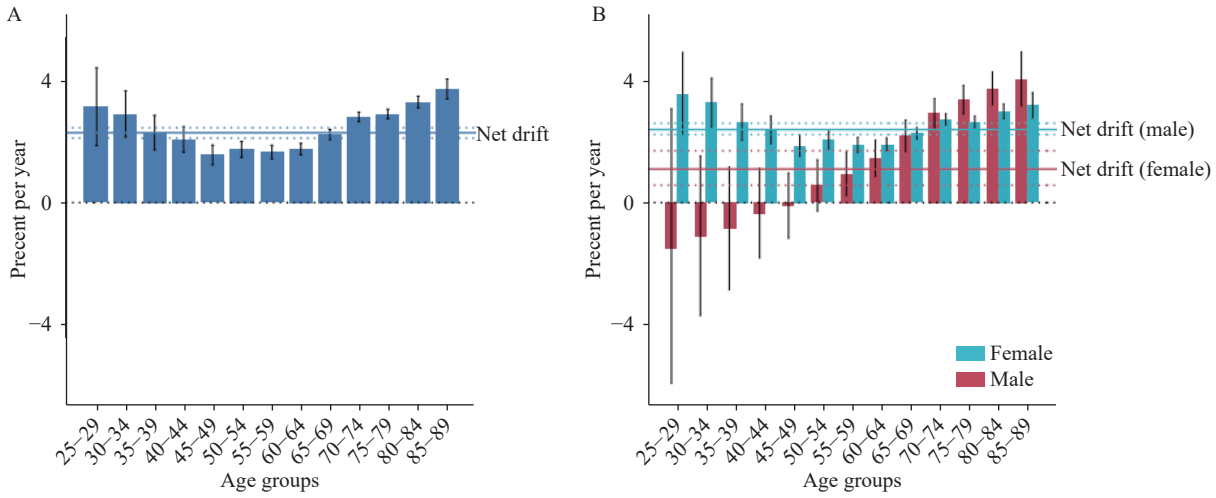


FIGURE 2. Net drift and local drift values for APMP-attributable CVD mortality in China. (A) Combined net and local drift values for both sexes; (B) Sex-stratified net and local drift values.
Note: Net drift represents the annual percentage change in expected age-adjusted rates over time; local drift indicates the annual percentage change in expected age-specific rates over time. The color bar displays local drift values by age group. Vertical bars indicate 95% *CI*. The horizontal colored line shows the net drift (solid line) with its 95% *CI* (dashed line). Abbreviation: APMP=ambient particulate matter pollution; CVD=cardiovascular disease; *CI*=confidence interval.

DISCUSSION

This study elucidated the long-term trends and underlying determinants of APMP-attributable CVD mortality in China. Between 1990 and 2021, age-standardized APMP-attributable CVD mortality increased substantially in both males and females. Although recent period effects showed favorable decreases in mortality risk, cohort analysis revealed a concerning pattern where mortality risk continued to rise in males across successive birth cohorts.

The age effect analysis demonstrated that APMP-attributable CVD mortality increased exponentially across age groups. This pattern reflects the heightened vulnerability of individuals with prolonged exposure to air pollution particles, compounded by age-related physiological changes that increase susceptibility to environmental influences (*7*). Given China's ongoing demographic transition and aging population, the CVD burden is projected to escalate (*8*). These findings underscore the critical need for targeted public health interventions to promote cardiovascular health among elderly populations, particularly those with extended exposure to ambient particulate matter pollution.

Period effects arise from external factors that uniformly influence all age groups during specific time intervals. Our analysis revealed a decrease in APMP-attributable CVD mortality risk in recent years, likely attributable to the implementation of comprehensive emission reduction policies and health promotion programs. The Air Pollution Prevention and Control Action Plan, implemented in China in 2013, achieved a 33.3% reduction in average annual APMP concentration by 2017. This initiative resulted in the prevention of 47,240 deaths through significant improvements in air quality (*9*).

Our findings demonstrated that the risk of APMP-attributable CVD mortality showed a consistent decline among females in birth cohorts after 1971. This reduction may be attributed to advances in CVD management, particularly improvements in early diagnosis and treatment protocols, combined with the substantial expansion of healthcare resources that has enabled broader access to essential medical services (*10*). However, these favorable trends were not observed in males, where mortality risk increased across successive birth cohorts. More targeted interventions are needed to address and reverse this concerning trend among male birth cohorts.

While this study provides valuable population-level insights into APMP-attributable CVD mortality trends, several limitations warrant consideration. First, as an ecological study, our population-level findings may not directly translate to individual-level associations. Second, APMP-attributable CVD mortality likely varies between rural and urban areas in China; however, we could not assess these geographic trends separately as the Global Burden of Disease

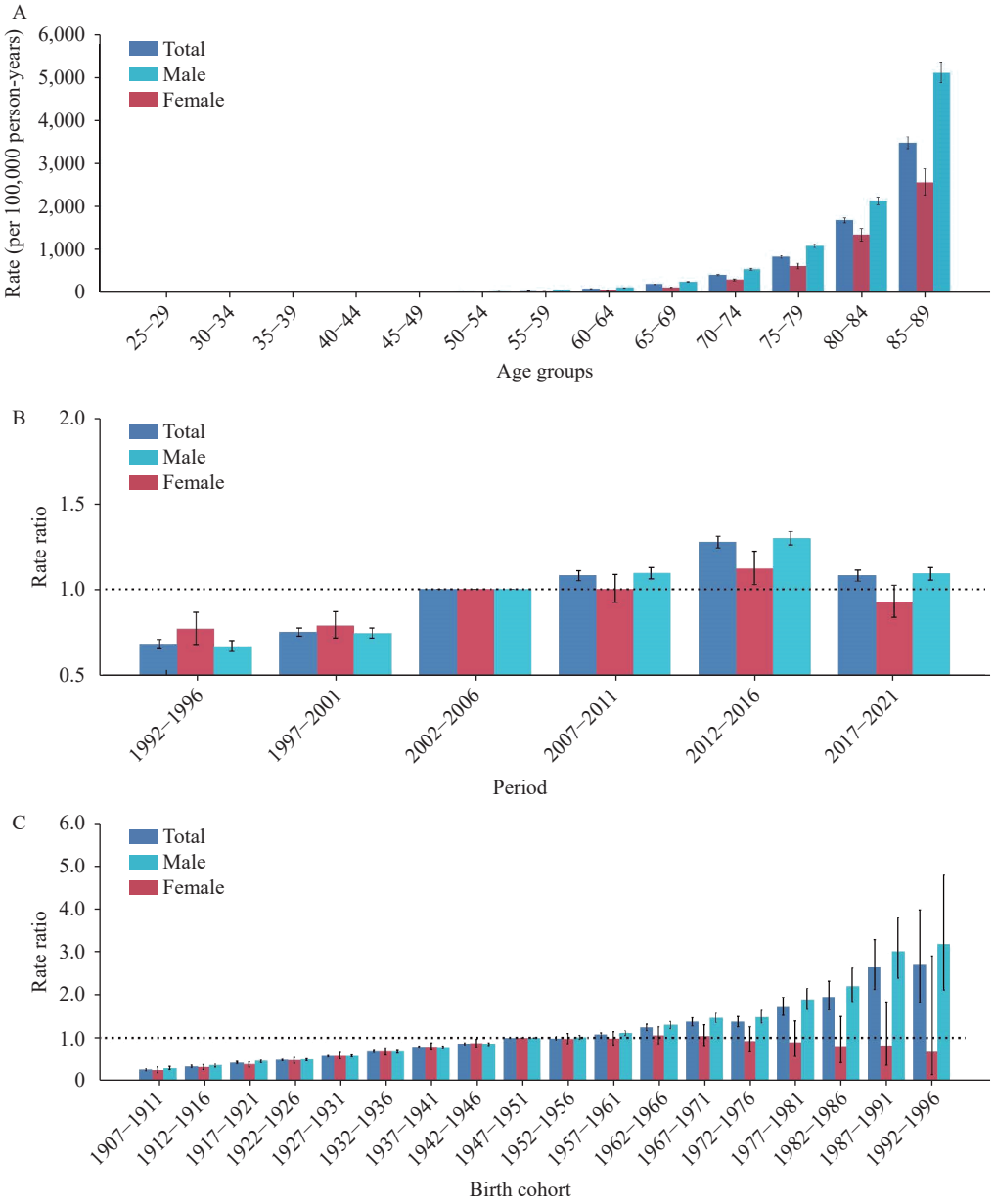


FIGURE 3. Age, period, and cohort effects on APMP-attributable CVD mortality in China. (A) Longitudinal age curves; (B) Period RR trends; (C) Cohort RR trends.
Note: Longitudinal age curves indicate age-specific effects. Vertical bars represent 95% confidence intervals (some intervals too narrow for visual display).
Abbreviation: APMP=ambient particulate matter pollution; CVD=cardiovascular disease; RR=relative risk.

Study does not disaggregate data by urbanization status. Despite these limitations, our findings provide crucial insights for future initiatives aimed at reducing APMP-attributable CVD mortality.

Conflicts of interest: No conflicts of interest.

Acknowledgements: Global Burden of Disease Study 2021 team and the National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention for their contributions.

doi: 10.46234/ccdcw2025.029

Corresponding author: Jing Wu, wujing@ncncd.chinacdc.cn.

[1] National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China; [2] Clinical Research Center, Children's Hospital of Nanjing Medical University, Nanjing City, Jiangsu Province, China.

Submitted: July 14, 2024
Accepted: January 09, 2025
Issued: January 31, 2025

REFERENCES

1. Mensah GA, Roth GA, Fuster V. The global burden of cardiovascular diseases and risk factors: 2020 and beyond. J Am Coll Cardiol 2019;74 (20):2529 – 32. https://doi.org/10.1016/j.jacc.2019.10.009.
2. The Writing Committee of the Report on Cardiovascular Health and Diseases in China. Interpretation of report on cardiovascular health and diseases in China 2022. Chin J Cardiovasc Med 2023;28(4):297 – 312. https://doi.org/10.3969/j.issn.1007-5410.2023.04.001.
3. Liang FC, Liu FC, Huang KY, Yang XL, Li JX, Xiao QY, et al. Long-term exposure to fine particulate matter and cardiovascular disease in China. J Am Coll Cardiol 2020;75(7):707 – 17. https://doi.org/10.1016/j.jacc.2019.12.031.
4. GBD 2021 Causes of Death Collaborators. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 2024;403 (10440):2100 – 32. https://doi.org/10.1016/S0140-6736(24)00367-2.
5. GBD 2021 Diseases and Injuries Collaborators. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 2024;403(10440):2133 – 61. https://doi.org/10.1016/S0140-6736(24)00757-8.
6. Rosenberg PS, Check DP, Anderson WF. A web tool for age-period-cohort analysis of cancer incidence and mortality rates. Cancer Epidemiol Biomarkers Prev 2014;23(11):2296 – 302. https://doi.org/10.1158/1055-9965.EPI-14-0300.
7. Al-Kindi SG, Brook RD, Biswal S, Rajagopalan S. Environmental determinants of cardiovascular disease: lessons learned from air pollution. Nat Rev Cardiol 2020;17(10):656 – 72. https://doi.org/10.1038/s41569-020-0371-2.
8. Gao YN, Huang HM, Ni CX, Feng Y, Yu JW, Huang YT, et al. Comparison of five expressions of handgrip strength for predicting cardiovascular disease risk factors in Chinese middle-aged community residents. Front Public Health 2022;10:903036. https://doi.org/10.3389/fpubh.2022.903036.
9. Huang J, Pan XC, Guo XB, Li GX. Health impact of China's air pollution prevention and control action plan: an analysis of national air quality monitoring and mortality data. Lancet Planet Health 2018;2(7): e313 – 23. https://doi.org/10.1016/S2542-5196(18)30141-4.
10. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. J Am Coll Cardiol 2017;70(1):1 – 25. https://doi.org/10.1016/j.jacc.2017.04.052.

Preplanned Studies

The Cohort Study on Association Between Prolonged Sleep Latency and Hypertension — 4 PLADs of the Southern China, 2018–2020

Li Xiang[1]; Jialu Yang[2]; Siqi Li[2]; Wanlan Chen[2]; Jiaqi Zhao[2]; Wanying Zhao[2]; Qi Zhang[2]; Min Xia[2]; Yan Liu[2,#]

Summary

What is already known about this topic?

Short sleep duration and poor sleep quality have been epidemiologically associated with cardiometabolic disorders. However, limited research has examined the relationship between prolonged sleep latency, an increasingly prevalent sleep disorder, and hypertension.

What is added by this report?

Approximately 25% of residents in 4 provincial-level administrative divisions (PLADs) in the southern China experienced prolonged sleep latency. Both occasional and habitual prolonged sleep latency were significantly associated with increased odds of hypertension.

What are the implications for public health practice?

Given the increasing prevalence of hypertension, health initiatives should focus on raising awareness about prolonged sleep latency and implementing targeted interventions to mitigate hypertension risk.

The prevalence of hypertension in China has risen dramatically to 23.2% over recent decades, driven by lifestyle changes and an aging population. Sleep disturbances, including short sleep duration, insomnia, and snoring, have emerged as significant risk factors for cardiometabolic disorders, including hypertension (*1*). Among these related disorders, prolonged sleep latency has become more prevalent in modern societies. However, the relationship between sleep latency and hypertension remains incompletely understood. Using baseline survey data from the South China Cohort (SCC) (*2*), this study analyzed 72,476 adults aged 25–89 years, with complete blood pressure and sleep behavior information. Hypertension was defined as either self-reported diagnosis/medication use or blood pressure measurements ≥140/90 mmHg. Sleep latency was assessed using the Pittsburgh Sleep Quality Index (PSQI) questionnaire. This analysis revealed a dose-dependent increase in hypertension prevalence corresponding to increasing frequency of prolonged sleep latency. After adjusting for potential covariates, logistic regression models demonstrated that individuals experiencing habitual prolonged sleep latency had a 21% higher prevalence of hypertension. These findings suggest that public health strategies targeting sleep latency should be implemented to help control the rising prevalence of hypertension.

This study utilized baseline survey data from the SCC, a prospective cohort study employing multistage, stratified cluster sampling across Guangdong, Fujian, Guangxi and Hainan Provinces between 2018 and 2020 (*2*). From 102,932 participants who completed face-to-face interviews, 30,456 participants were excluded due to missing information on sleep behaviors (n=27,738) or hypertension (n=2,718), yielding a final analytical sample of 72,476 participants (Supplementary Figure S1, available at https://weekly.chinacdc.cn/). Comparisons of major socio-economic characteristics between included and excluded participants are presented in Supplementary Table S1 (available at https://weekly.chinacdc.cn/). Sleep latency was assessed using two questions: "During the past month, how long has it taken you to fall asleep each night? (0=falling asleep in ≤15 min, 1=16 to 30 min, 2=31 to 60 min, and 3=over 60 min)", and "During the past month, how often have you had trouble sleeping because you cannot get to sleep within 30 min? (0=none during the past month, 1=less than once a week, 2=once or twice a week, and 3=three or more times a week)". Based on the composite score of these two questions, prolonged sleep latency was categorized as normal (0–2 points), occasional (3–4 points), or habitual (5–6 points) (Supplementary Table S2, available at https://weekly.chinacdc.cn/). Hypertension was defined according to Chinese Guidelines for the Prevention and Treatment of Hypertension as either prior physician diagnosis from tertiary hospitals, current antihypertensive medication use within two

weeks, or blood pressure measurements ≥140/90 mmHg (*3*). The study protocol was approved by the Ethics Committee of School of Public Health, Sun Yat-Sen University (L2017-001).

Normally distributed continuous data were presented as mean±standard deviation (SD), while skewed data were expressed as median with the interquartile range (P_{25}–P_{75}). One-way analysis of variance was employed for continuous variables, and the chi-squared (χ^2) tests were used for categorical variables. Linear trends across sleep latency categories were assessed using linear regression model for continuous variables and the Cochran-Armitage trend test for categorical variables. The association between prolonged sleep latency and hypertension was evaluated using logistic regression models with sleep latency categorized as normal, occasional, or habitual. The relationship between sleep latency and hypertension was further modeled using restricted cubic splines. To ensure result robustness, multiple sensitivity analyses and subgroup analyses were conducted as detailed in the Supplementary Material (available at https://weekly.chinacdc.cn/). All statistical tests were two-tailed, with *P* value <0.05 considered statistically significant. Analyses were performed using R version 4.2.0 (The R Foundation for Statistical Computing, Vienna, Austria).

Among the 72,476 study participants, 17,416 (24.03%) had hypertension, and 18,170 (25.07%) experienced prolonged sleep latency. Compared to participants with normal sleep latency (*n*=54,306), those with prolonged sleep latency (*n*=18,170) were older, more likely to be female, exhibited more unhealthy lifestyle behaviors and adverse metabolic profiles (*P* for trend <0.001). Notably, individuals with prolonged sleep latency also had significantly shorter sleep duration (6.97 and 6.30 hours *vs*. 7.16 hours, *P* for trend <0.001), and reported poorer overall sleep quality (64.53% and 42.09% *vs*. 92.25% of proportion of good sleep quality, *P* for trend <0.001, Table 1). In multivariable-adjusted analyses, sleep latency score demonstrated a linear association with hypertension prevalence (*P* for nonlinearity =0.010, Figure 1). Compared to those with normal sleep latency, the fully adjusted odds ratio (*OR*) and 95% confidence interval (*CI*) for hypertension among those with occasional and habitual prolonged sleep latency were 1.10 (1.03, 1.17), and 1.21 (1.14, 1.29), respectively (Table 2, Model 3). The individual components of prolonged sleep latency — both taking longer to fall asleep (exceeding 30 min) and experiencing multiple instances of sleep initiation difficulty — showed independent associations with increased odds of hypertension (Supplementary Table S3, available at https://weekly.chinacdc.cn/).

The adverse association between habitual prolonged sleep latency and hypertension remained consistent across various subgroups stratified by sex, age, central obesity status and lifestyle factors. However, the impact of occasional prolonged sleep latency on hypertension prevalence was more pronounced among women, individuals with central obesity and those using sleep-aiding medications (Supplementary Table S4, available at https://weekly.chinacdc.cn/). Furthermore, sensitivity analyses yielded consistent results when using alternative hypertension definitions (SBP/DBP ≥ 130/80 mmHg), and when restricting analyses to previously diagnosed hypertension cases (Supplementary Table S3).

DISCUSSION

In contemporary societies, prolonged sleep latency represents a pervasive yet frequently underdiagnosed and undertreated sleep disorder. Analysis of the SCC baseline data revealed that over one quarter of the study participants experienced prolonged sleep latency. The findings demonstrated that occasional and habitual prolonged sleep latency was associated with 10% and 21% higher odds of hypertension prevalence, respectively. These results identify prolonged sleep latency served as a modifiable risk factor for hypertension that warrants increased attention.

While sleep is fundamental for maintaining both physical and mental health, epidemiological investigations of sleep-related cardiometabolic complications have predominantly focused on sleep duration, overlooking the impact of prolonged sleep latency — a more prevalent sleep disorder in modern societies. This finding aligns with a previous cross-sectional study that demonstrated an association between longer night sleep latency and increased odds of hypertension (*4*). The present study extends these observations by confirming this relationship in a substantially larger cohort while controlling for established cardiometabolic risk factors. The robust sample size enabled subgroup analyses across various demographic and lifestyle characteristics, validating the consistency of this association. Similar relationships have been documented in other populations, with prolonged sleep-onset latency with a 60% higher probability of cardiovascular diseases in the US

TABLE 1. Baseline characteristics of study participants stratified by sleep latency status in Four PLADs of South China, 2018–2020.

Characteristic	Overall (*n*=72,476)	Normal latency (*n*=54,306)	Prolonged latency		*P* for trend
			Occasional (*n*=9,341)	Habitual (*n*=8,829)	
Age*, years	56.53 (11.69)	55.85 (11.63)	58.57 (11.64)	58.55 (11.61)	<0.001
Female†, *n* (%)	43,255 (59.68)	31,173 (57.40)	6,132 (65.65)	5,950 (67.39)	<0.001
Married, *n* (%)	56,516 (77.98)	43,511 (80.12)	6,244 (66.85)	6,761 (76.58)	<0.001
Han ethnic group, *n* (%)	51,010 (78.69)	37,928 (79.43)	6,528 (77.87)	6,554 (75.40)	<0.001
Higher education, *n* (%)	27,476 (37.91)	21,654 (39.87)	3,641 (38.98)	2,181 (24.70)	<0.001
Retirement, *n* (%)	27,563 (38.03)	19,854 (36.56)	4,650 (49.78)	3,059 (34.65)	<0.001
Income less than 150,000 Chinese Yuan, *n* (%)	63,836 (88.08)	48,208 (88.77)	7,869 (84.24)	7,759 (87.88)	<0.001
Lifestyle behaviors					
Current smoking, *n* (%)	10,723 (14.80)	8,328 (15.34)	1,151 (12.32)	1,244 (14.09)	<0.001
Current drinking, *n* (%)	22,761 (31.40)	16,916 (31.15)	2,504 (26.81)	3,341 (37.84)	<0.001
Regular exercise, *n* (%)	7,624 (10.52)	5,127 (9.44)	1,621 (17.35)	876 (9.92)	<0.001
Physical and clinical measurements					
Waist circumference, cm	82.25 (9.59)	82.34 (9.62)	81.79 (9.48)	82.20 (9.46)	<0.001
BMI, kg/m^2	23.91 (3.43)	23.97 (3.43)	23.75 (3.44)	23.65 (3.40)	<0.001
SBP, mmHg	128.88 (19.20)	128.61 (19.14)	128.68 (19.24)	130.78 (19.47)	<0.001
DBP, mmHg	77.94 (12.30)	78.10 (12.34)	75.89 (11.96)	79.13 (12.13)	<0.001
Triglycerides§, mmol/L	1.28 (0.90, 1.86)	1.27 (0.90, 1.86)	1.30 (0.91, 1.90)	1.28 (0.91, 1.86)	0.646
Total cholesterol, mmol/L	5.27 (4.59, 6.01)	5.26 (4.59, 6.00)	5.30 (4.61, 6.06)	5.29 (4.60, 6.05)	<0.001
HDL-c, mmol/L	1.43 (1.18, 1.72)	1.43 (1.19, 1.73)	1.43 (1.18, 1.74)	1.41 (1.17, 1.68)	<0.001
LDL-c, mmol/L	3.13 (2.58, 3.75)	3.12 (2.58, 3.74)	3.16 (2.57, 3.82)	3.17 (2.57, 3.78)	<0.001
Comorbidities					
Hypertension, *n* (%)	17,416 (24.03)	12,343 (22.73)	2,530 (27.08)	2,543 (28.80)	<0.001
Diabetes, *n* (%)	4,933 (12.37)	3,489 (12.01)	727 (12.60)	717 (14.16)	<0.001
Cardiovascular disease, *n* (%)	2,724 (3.76)	1,796 (3.31)	441 (4.72)	487 (5.52)	<0.001
Cancer, *n* (%)	732 (1.84)	508 (1.75)	116 (2.01)	108 (2.14)	0.099
Sleep behaviors					
Time to fall asleep, minutes	20.85 (22.00)	13.04 (8.81)	32.85 (20.02)	56.13 (36.04)	<0.001
Difficulty falling asleep, *n* (%)	9,011 (12.43)	0 (0.00)	899 (9.62)	8,112 (91.88)	<0.001
Sleep duration, hours	7.03 (1.27)	7.16 (1.16)	6.97 (1.30)	6.30 (1.59)	<0.001
Good sleep quality, *n* (%)	59,842 (82.57)	50,098 (92.25)	6,028 (64.53)	3,716 (42.09)	<0.001
Medication for sleep, *n* (%)	2,351 (3.24)	1,027 (1.42)	649 (6.95)	675 (7.65)	<0.001
Habit of Napping, *n* (%)	41,968 (57.90)	31,385 (57.80)	5,470 (58.56)	5,113 (57.91)	0.427

Abbreviation: BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure, HDL-c=high-density lipoprotein cholesterol, LDL-c=low-density lipoprotein cholesterol; SD=standard deviation.

* Normally distributed continuous data were presented as mean±SD.

† Categorical variables were expressed as cases (Percent).

§ Skewed data were expressed as median with the interquartile range (P_{25}–P_{75}).

population (*5*), and each 10-minute increase in sleep latency corresponding to an 89% increase in hypertension risk among police officers (*6*). While previous research has identified prolonged sleep latency as an indicator of sleep disorders and reduced sleep efficiency (*7*), most studies have focused solely on time to fall asleep, neglecting the frequency and chronicity of the condition. To address this limitation, this study developed a more comprehensive sleep latency score incorporating both the time to fall asleep and

frequency of sleep initiation difficulties. The results revealed that habitual prolonged sleep latency was more prevalent among elderly individuals, women, and subjects with lower educational and economic status. Furthermore, prolonged sleep latency frequently co-occurred with shorter sleep duration and diminished self-reported sleep quality. Notably, after adjusting for these confounding factors, habitual prolonged sleep latency maintained a significant association with a 21% higher likelihood of having hypertension. This detrimental effect persisted across both genders, all age groups, and varying levels of healthy lifestyle adherence. Additionally, we observed that occasional prolonged sleep latency had a more pronounced adverse effect in females and subjects with central obesity, suggesting heightened vulnerability in these populations. While the molecular mechanisms linking prolonged sleep latency to hypertension remain incompletely understood, the observed association may be explained by physiological alterations, including sympathetic nervous system activation, disruption of the hypothalamic-pituitary-adrenal axis affecting cortisol secretion and renin-angiotensin system activity, and elevated systemic inflammation (*8*).

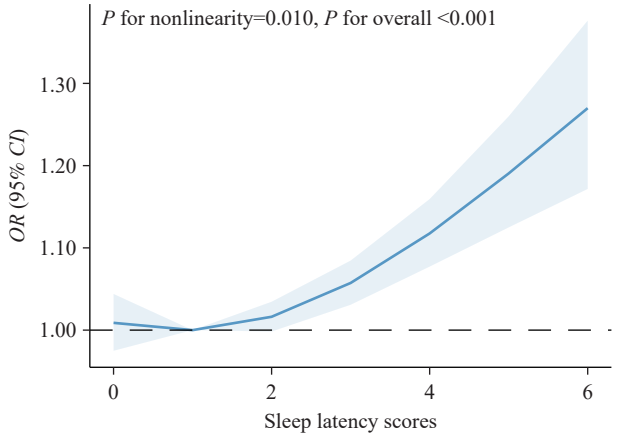


FIGURE 1. Restricted cubic spline for the association between sleep latency and hypertension among adults in South China, 2018–2020.
Note: The *OR* was adjusted for age, gender, education level, income, ethnic group, body mass index, smoking, drinking, regular exercise and self-reported sleep quality.
Abbreviation: *OR*=odds ratio; *CI*=confidence interval.

Several limitations warrant consideration in interpreting these findings. Although the results remained robust across multiple sensitivity analyses, the cross-sectional design precludes definitive causal inference. Future prospective studies across diverse populations are needed to establish causality. Additionally, while self-reported sleep behaviors and lifestyle data are wildly used and validated in large-scale population studies, the potential for misclassification and recall bias cannot be eliminated. Finally, the exclusion of approximately 38% of participants due to missing sleep behavior and hypertension data represents a notable limitation. However, the substantial sample size and consistent findings across sensitivity analyses support the robustness of the conclusions in this study.

In conclusion, the findings underscore the importance of increasing public awareness regarding the adverse effects of prolonged sleep latency on hypertension risk and support the integration of sleep management into current lifestyle intervention strategies for hypertension prevention and control.

Acknowledgments: We are grateful to all participants who contributed to this research. The study protocol was approved by the Ethics Committee of School of Public Health, Sun Yat-Sen University (L2017-001). Informed consent was obtained from all participants.

Conflicts of interest: No conflicts of interest.

Funding: Supported by the Guangzhou Science and Technology Project (2024A04J6477) and the Fundamental Research Funds for the Central

TABLE 2. Association between prolonged sleep latency and hypertension among adults in Four PLADs of South China, 2018-2020, multivariable logistic regression analyses.

Prolonged sleep latency	Hypertension (%)	Crude model		Model 1*		Model 2†		Model 3§	
		OR (95% *CI*)	*P*	*OR* (95% *CI*)	*P*	*OR* (95% *CI*)	*P*	*OR* (95% *CI*)	*P*
Normal	12,343 (22.73)	1		1		1		1	
Occasional	2,530 (27.08)	1.26(1.20,1.33)	<0.001	1.05(0.99,1.11)	0.065	1.09(1.03,1.15)	0.004	1.10(1.03,1.17)	0.003
Habitual	2,543 (28.80)	1.38(1.31,1.45)	<0.001	1.16(1.10,1.23)	<0.001	1.23(1.16,1.30)	<0.001	1.21(1.14,1.29)	<0.001

Abbreviation: *OR*=odds ratio, *CI*=confidence interval; Ref.=reference.
* Model 1: Adjusted for age and sex.
† Model 2: Adjusted for age, sex, education level, income, and ethnicity.
§ Model 3: Adjusted for age, sex, education level, income, ethnicity, body mass index, smoking status, alcohol consumption, regular exercise, and self-reported sleep quality.

University (Sun Yat-sen University, 22hytd03).

doi: 10.46234/ccdcw2025.030

[#] Corresponding author: Yan Liu, liuyan215@mail.sysu.edu.cn.

[1] Guangdong Provincial Key Laboratory of Food, Nutrition and Health, and Department of Statistics and Epidemiology, School of Public Health, Sun Yat-sen University, Guangzhou City, Guangdong Province, China; [2] Guangdong Provincial Key Laboratory of Food, Nutrition and Health, and Department of Nutrition, School of Public Health, Sun Yat-sen University, Guangzhou City, Guangdong Province, China.

Submitted: August 20, 2024
Accepted: January 05, 2025
Issued: January 31, 2025

REFERENCES

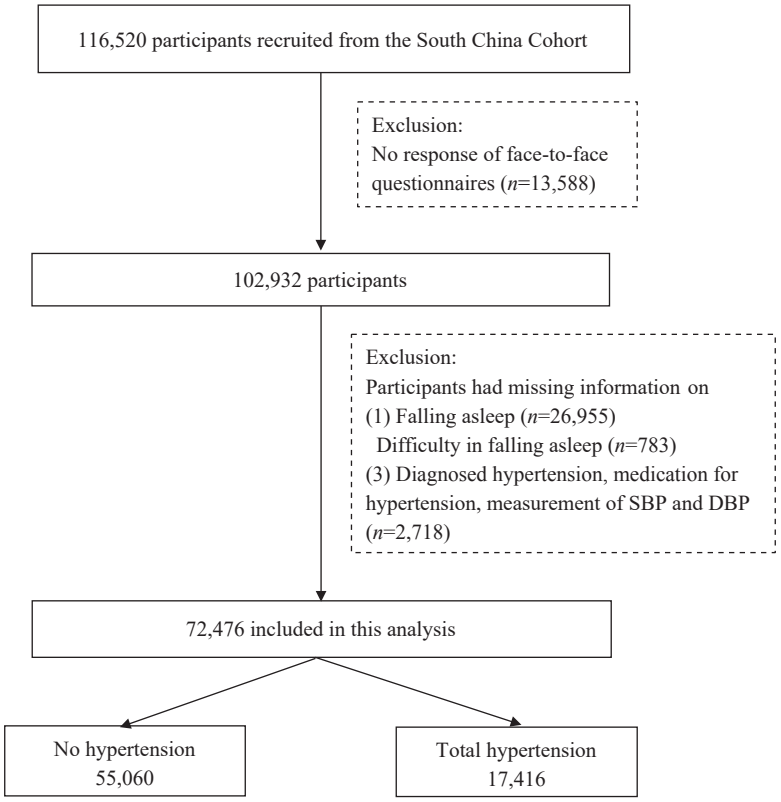
1. Meng L, Zheng Y, Hui RT. The relationship of sleep duration and insomnia to risk of hypertension incidence: a meta-analysis of prospective cohort studies. Hypertens Res 2013;36(11):985 – 95. https://doi.org/10.1038/hr.2013.70.
2. Yang JL, Luo SY, Liu Y, Hong MH, Qiu XQ, Lin YZ, et al. Cohort profile: South China cohort. Int J Epidemiol 2024;53(2):dyae028. https://doi.org/10.1093/ije/dyae028.
3. Joint Committee for Guideline Revision. 2018 Chinese guidelines for prevention and treatment of hypertension-a report of the revision committee of Chinese guidelines for prevention and treatment of hypertension. J Geriatr Cardiol 2019;16(3):182 – 241. https://doi.org/10.11909/j.issn.1671-5411.2019.03.014.
4. Zhong X, Gou FY, Jiao HC, Zhao DS, Teng J. Association between night sleep latency and hypertension: a cross-sectional study. Medicine (Baltimore) 2022;101(42):e31250. https://doi.org/10.1097/md.0000000000031250.
5. Kadier K, Qin L, Ainiwaer A, Rehemuding R, Dilixiati D, Du YY, et al. Association of sleep-related disorders with cardiovascular disease among adults in the United States: a cross-sectional study based on national health and nutrition examination survey 2005-2008. Front Cardiovasc Med 2022;9:954238. https://doi.org/10.3389/fcvm.2022.954238.
6. Ma CC, Gu JK, Bhandari R, Charles LE, Violanti JM, Fekedulegn D, et al. Associations of objectively measured sleep characteristics and incident hypertension among police officers: the role of obesity. J Sleep Res 2020;29(6):e12988. https://doi.org/10.1111/jsr.12988.
7. Kang I, Kim S, Kim BS, Yoo J, Kim M, Won CW. Sleep latency in men and sleep duration in women can be frailty markers in community-dwelling older adults: the korean frailty and aging cohort study (KFACS). J Nutr Health Aging 2019;23(1):63 – 7. https://doi.org/10.1007/s12603-018-1109-2.
8. Meier-Ewert HK, Ridker PM, Rifai N, Regan MM, Price NJ, Dinges DF, et al. Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. J Am Coll Cardiol 2004;43(4):678 – 83. https://doi.org/10.1016/j.jacc.2003.07.050.

SUPPLEMENTARY MATERIAL

eMethods

Covariates assessment Comprehensive covariate data were collected through structured questionnaires. Marital status was categorized as married or widowed/divorced/separated/unmarried. Educational attainment was dichotomized into high school completion or above. Household was classified as above or below 150,000 Chinese Yuan. Current smoking status was defined as regular consumption of ≥1 cigarette daily or ≥7 cigarettes weekly during the previous 6 months. Current alcohol consumption was defined as regular intake ≥once weekly during the past 12 months.. Regular physical activity was defined as ≥150 minutes/week of moderate-intensity activity, ≥75 minutes/week of vigorous-intensity aerobic activity, or an equivalent combination thereof. Central obesity was defined using waist-to-hip ratio thresholds of ≥0.90 for males and ≥0.85 for females, based on established criteria. For blood pressure measurements, participants rested for 5 minutes before two seated measurements were taken using a digital automatic analyzer (Omron HEM-7136) with a 2-minute interval. A third measurement was required if the difference in systolic blood pressure (SBP) or diastolic blood pressure (DBP) between measurements exceeded 10 mmHg (1 mmHg=0.133 kPa). The mean of the final two measurements was used for analysis.

Subgroup analysis and sensitivity analysis To assess the robustness of our findings, we conducted stratified analyses by gender, age (<65, ≥65 years), current smoking status, alcohol consumption, regular exercise, central obesity and use of sleep-aiding medications. Additionally, two sensitivity analyses were performed: first, redefining hypertension using the 2017 American College of Cardiology/American Heart Association guideline threshold of ≥130/80 mmHg; and second, restricting the definition to previously diagnosed hypertension only.



SUPPLEMENTARY FIGURE S1. Flow chart of this study in four PLADs of South China, 2018–2020.

SUPPLEMENTARY TABLE S1. Comparison of basic characteristics between analyses participants and missed participants from four PLADs of South China, 2018–2020.

Characteristics	Analyses participants (*N*=72,476)	Missed participants (*N*=30,456)	*P*
Age, years	56.53 (11.69)	53.49 (12.95)	0.017
Female, *n* (%)	43,255 (59.68)	19,403 (63.71)	<0.001
Married, *n* (%)	56,516 (77.98)	27,008 (89.38)	<0.001
Higher education, *n* (%)	27,476 (37.91)	11,623 (38.29)	0.449
Less than 150,000 Chinese Yuan, *n* (%)	63,836 (88.08)	26,922 (88.40)	0.153
Retirement, *n* (%)	27,563 (38.03)	11,756 (38.60)	0.087
Han ethnic group, *n* (%)	51,010 (70.38)	29,893 (98.15)	<0.001

SUPPLEMENTARY TABLE S2. The definition of sleep latency score among adults in four PLADs of South China, 2018–2020.

Difficulty falling asleep Time to fall asleep	0 time/week (0 point)	<1 time/week (1 point)	1–2 times/week (2 points)	>3 times/week (3 points)
Fall asleep ≤15 minutes (0 point)	0	1	2	3
Fall asleep 16–30 minutes (1 point)	1	2	3	4
Fall asleep 31–60 minutes (2 points)	2	3	4	5
Fall asleep >60 minutes (3 points)	3	4	5	6

SUPPLEMENTARY TABLE S3. The association between sleep latency components and hypertension among adults in four PLADs of South China, 2018–2020.

Sleep latency components	Number of hypertension	Crude model		Model 1*		Model 2†		Model 3§	
		OR (95% *CI*)	*P*	*OR* (95% *CI*)	*P*	*OR* (95% *CI*)	*P*	*OR* (95% *CI*)	*P*
Time to fall asleep									
≤15 minutes	7,940 (22.77%)	1		1		1		1	
16–30 minutes	3,366 (24.46%)	1.10 (1.05,1.15)	<0.001	0.93 (0.88,0.97)	0.002	0.90 (0.85,0.95)	<0.001	0.92 (0.87,0.98)	0.006
31–60 minutes	4,351 (24.28%)	1.09 (1.04,1.13)	<0.001	1.01 (0.97,1.06)	0.586	1.04 (0.99,1.09)	0.123	1.06 (1.01,1.12)	0.021
>60 minutes	1,759 (30.29%)	1.43 (1.35,1.52)	<0.001	1.16 (1.09,1.24)	<0.001	1.25 (1.16,1.33)	<0.001	1.23 (1.14,1.33)	<0.001
Difficulty falling asleep									
None during the past month	10,367 (21.56%)	1		1		1		1	
Less than once a week	2,857 (29.85%)	1.55 (1.47,1.63)	<0.001	1.10 (1.05,1.16)	<0.001	1.09 (1.03,1.15)	0.004	1.12 (1.06,1.19)	<0.001
Once or twice a week	1,626 (27.95%)	1.41 (1.33,1.50)	<0.001	1.05 (0.98,1.12)	0.166	1.09 (1.02,1.17)	0.015	1.09 (1.01,1.17)	0.026
Three or more times a week	2,566 (28.48%)	1.45 (1.38,1.52)	<0.001	1.15 (1.09,1.22)	<0.001	1.22 (1.15,1.29)	<0.001	1.19 (1.12,1.27)	<0.001
Prolonged Sleep latency (sensitivity analysis 1)									
Normal	12,343 (22.73%)	1		1		1		1	
Occasional	2,530 (27.08%)	1.19 (1.14,1.25)	<0.001	0.99 (0.91,1.04)	0.729	1.04 (0.98,1.10)	0.152	1.05 (0.99,1.12)	0.085
Habitual	2,543 (28.80%)	1.29 (1.23,1.35)	<0.001	1.09 (1.03,1.15)	0.002	1.22 (1.16,1.29)	<0.001	1.19 (1.12,1.26)	<0.001
Prolonged Sleep latency (sensitivity analysis 2)									
Normal	10,736 (19.77%)	1		1		1		1	
Occasional	2,305 (24.68%)	1.33 (1.26,1.40)	<0.001	1.11 (1.05,1.17)	<0.001	1.12 (1.05,1.18)	<0.001	1.11 (1.05,1.19)	<0.001
Habitual	2,351 (26.63%)	1.47 (1.40,1.55)	<0.001	1.25 (1.19,1.33)	<0.001	1.23 (1.16,1.30)	<0.001	1.22 (1.14,1.30)	<0.001

Abbreviation: *OR*=odds ratio; *CI*=confidence interval.

* Model 1: Adjusted for age and sex.

† Model 2: Adjusted for age, sex, education level, income, and ethnicity.

§ Model 3: Adjusted for age, sex, education level, income, ethnicity, body mass index, smoking status, alcohol consumption, regular exercise, and self-reported sleep quality.

SUPPLEMENTARY TABLE S4. The association of sleep latency with hypertension in different subgroups among adults in four PLADs of South China, 2018–2020.

Subgroup	Number of hypertension	Normal	Occasional prolonged		Habitual prolonged		*P* for interaction
		*OR** (95% *CI*)	*OR** (95% *CI*)	*P*	*OR** (95% *CI*)	*P*	
Sex							0.002
Male	6,822 (39.17%)	1	1 (0.89,1.09)	0.827	1.15 (1.03,1.28)	0.011	
Female	10,594 (60.83%)	1	1.15 (1.07,1.25)	<0.001	1.25 (1.15,1.35)	<0.001	
Age group							0.241
<65 years	8,462 (48.59%)	1	1.14 (1.05,1.24)	0.002	1.24 (1.13,1.35)	<0.001	
≥65 years	8,954 (51.41%)	1	1.20 (1.10,1.30)	<0.001	1.37 (1.25,1.49)	<0.001	
Smoking							0.041
Yes	1,930 (11.08%)	1	0.92 (0.77,1.11)	0.407	1.24 (1.04,1.48)	0.016	
No	15,486 (88.92%)	1	1.12 (1.05, 1.19)	<0.001	1.21 (1.13,1.29)	<0.001	
Drinking							0.293
Yes	6,139 (35.25%)	1	1.06 (0.95,1.18)	0.320	1.27 (1.14,1.40)	<0.001	
No	11,277 (64.75%)	1	1.11 (1.03,1.20)	0.004	1.18 (1.09,1.28)	<0.001	
Regular exercise							0.084
Yes	2,874 (16.50%)	1	1.22 (1.07,1.39)	0.003	1.29 (1.09,1.53)	0.003	
No	14,542 (83.50%)	1	1.06 (0.99,1.14)	0.078	1.20 (1.12,1.28)	<0.001	
Central obesity							0.856
Yes	10,268 (59.96%)	1	1.10 (1.01,1.19)	<0.001	1.20 (1.10,1.30)	<0.001	
No	7,148 (41.04%)	1	1.06 (0.97,1.63)	0.197	1.18 (1.08,1.30)	<0.001	
Medication for sleep							<0.001
Yes	620 (3.56%)	1	1.13 (1.06,1.21)	<0.001	1.19 (1.10,1.30)	<0.001	
No	16,774 (96.44%)	1	0.87 (0.66,1.15)	0.340	1.51 (1.15,1.99)	<0.001	

Abbreviation: *OR*=odds ratio; *CI*=confidence interval.

* The *OR* was adjusted for age, sex, education level, income, ethnicity, body mass index, smoking status, alcohol consumption, regular exercise, and self-reported sleep quality. Stratification criteria were excluded from its group.

Youth Editorial Board

Indexed by Science Citation Index Expanded (SCIE), Social Sciences Citation Index (SSCI), PubMed Central (PMC), Scopus, Chinese Scientific and Technical Papers and Citations, and Chinese Science Citation Database (CSCD)

The inauguration of *China CDC Weekly* is in part supported by Project for Enhancing International Impact of China STM Journals Category D (PIIJ2-D-04-(2018)) of China Association for Science and Technology (CAST).

CCDC weekly

Vol. 7 No. 5 Jan. 31, 2025

Responsible Authority
National Disease Control and Prevention Administration

Sponsor
Chinese Center for Disease Control and Prevention

Editing and Publishing
China CDC Weekly Editorial Office
No.155 Changbai Road, Changping District, Beijing, China
Tel: 86-10-63150501, 63150701
Email: weekly@chinacdc.cn

CSSN
ISSN 2096-7071 (Print)
ISSN 2096-3101 (Online)
CN 10-1629/R1