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Spatial and Demographic Disparities in Short Stature among Schoolchildren aged 7-18 years: a Nation-wide Survey in China, 2014

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	Keywords:	short stature, prevalence, China, spatial disparities, demographic disparities

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Spatial and Demographic Disparities in Short Stature among Schoolchildren aged 7-18 years: a Nation-wide Survey in China,

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Abstract

Objectives:Aiming to identify spatial disparities and demographic characteristics of short stature, we analyzed the prevalence of short stature collected in a nation-wide health survey.

Settings:Data were obtained from the 2014 Chinese National Survey on Students Constitution and Health .Students selected from 30 provinces, autonomous regions and municipalities (except Tibet, Hong Kong, Macao and Taiwan).

Participants: There are 213,795 Han students between 7-18 years old enrolled in our study, all participants were selected by stratified cluster sampling.

Primary and secondary outcome measures:short stature(China's age- and gender-specific height growth charts were used for short stature assessment).

Results: The age-standardized prevalence of short stature nationwide were 3.70% according to China growth chart. The short stature prevalence differed greatly among age groups, urban-rural areas, and regions with different economic development (all p<0.0001), especially in areas (2.23% in urban vs 5.12% in rural areas, p<0.001) and regions (2.60 in developed, 3.72% in intermediately developed, 4.69% in under-developed regions, p<0.0001). The spatial distribution of short stature prevalence exhibited a clustered pattern. Moran's I value was 0.474(P < 0.001). The southwest part of China showed higher short stature prevalence, whereas lower short stature prevalence was observed mainly in the northeast part of China.

Conclusions:There is a significant highly prevalence of short stature in rural, intermediately developed, under-developed areas of China, this would provide corroborating evidence for tailored strategy on short stature prevention and reduction in special areas. We also uncover that there is spatial clusters of short stature in the southwestern China, therefore further study needs to be done in these places to detected the cause of short stature. It indicates that except for racial factor, the regional factor maybe be need to considered when we define short stature.

Strengths and limitations of this study

This is the first study to detect the spatial discrepancy of short stature prevalence in China.

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This study did not evaluate the short stature of minorities. There are 56 minorities in China, it maybe meaningful to know the condition of short stature in these minorities to see if there is any different to other people who live in same geographical environment.

The prevalence of short stature may be overestimated in some area such as Sichuan,Guizhou,Guangxi,Chongqing,Hainan,Yunnan provinces,do we need to make the special diagnostic criteria for these places or we must be more prudent when we diagnose short stature of children from these areas.

Introduction

Short stature is a major morbid condition for children who are referred to pediatric endocrinologists. About half of new visits to pediatric endocrine department are harassed by short stature¹. It is usually caused by multiple factors, including children's nutritional status, psychological well-being and existence of several unknown metabolic disorders. Short stature's causes are wide spectrum and mainly divided into normal (e.g. familial short stature, constitutional delay of growth) and pathological(e.g., growth hormone deficiency, Turner syndrome, hypothyroidism, chronic diseases, idiopathic short stature, etc.)². A large number of children with short stature are unaware of their morbid status and some of their causes remained unidentified. With the advancement of molecular diagnostic techniques, some unexplained short stature are gradually revealed. It can somewhat be attributed to genetic variation, indicating short stature as a phenotype of genetic diseases. Additionally, short stature affects children's physical and mental health. Children with short stature tend to suffer psychological disorders, such as low self-esteem, depression, social immaturity, behavioral problems, and academic difficulties³. Short stature can still affect children's health after they grow up, for instance, females with short stature were susceptible to have preterm birth when they became pregnant in adulthood⁴. Therefore, identifying short stature in childhood is

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extremely important for physical and mental illness reduction and it should be an imperative part of children's health programs.

Short stature varied greatly among different regions due to diverse social development and natural environment⁵⁻⁸. It has been reported that children living in undeveloped areas were more likely to have stunted growth and short stature was highly prevalent, United Nations International Children's Emergency Fund data showed in 2017, the prevalence of stunting under 5 years old in eastern and South Africa and South Asia were 34.1%, 35%, respectively⁹. In addition, children living in economically developed areas but with low latitude were also susceptible to short stature¹⁰, indicating that geographical factors may play an important role in short stature. In mainland China, children in North had higher height than children in South on average¹¹. As diagnosis of short stature is based on growth height, spatial disparities in height may suggest same trend in prevalence of short stature among different areas, but when we diagnose short stature we need to exclude this kind of natural environment factors and avoiding overestimate the prevalence of short stature, avoiding excessive laboratory tests or therapy for children. Unfortunately, data related to geographical distribution of short stature is seldomly reported. To fill in such gap, we analyzed the schoolchildren's height in a nation-wide health survey, aiming to identify spatial disparities and demographic characteristics of short stature.

Methods

Date collection and sampling

Data were collected from the 2014 Chinese National Survey on Students Constitution and Health (CNSSCH), a nationally health survey on schoolchildren. Eligible participants were Han, Chinese people aged 7-18 years old. The sampling procedures of CNSSCH have been published¹². In a word, all participants were selected by stratified cluster sampling according to the principle of CNSSCH. Selected places in each

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provinces were graded into developed, intermediately developed, under-developed levels based on the local economic development. Subsequently, children were divided into four strata: urban boys, urban girls, rural boys and rural girls. Then 50 people were selected in each unit (per years old. gender, urban/rural, Developed/Intermediately developed/Under-developed, province). In the end, 213795 Han students were enrolled in our study, and they came from 30 provinces, autonomous regions or municipalities (except Tibet, Hong Kong, Macao and Taiwan). The 18 years old schoolchildren of Beijing did not divide into 3 classes based on the condition of economic development, so we excluded the data of this group.

Patient and Public Involvement

This study was conducted in accordance with the guidelines laid down in the Helsinki declaration, meanwhile this study has approved by six ministries of China. We obtained informed consent from parents and students. This study was approved by the Medical Research Ethics Committee of Peking University Health Science Center (IRB00001052–13082), and Clinical research ethics committee of China-Japan friendship hospital(2018-93-K67).

Anthropometric Measurements

Standing height (cm) was measured by trained staff following a standardized procedure, which was in accordance with anthropometry methods in 2006 World Health Organization (WHO) Child Growth Standards. Height was measured to the nearest 0.1 cm with portable stadiometers. Children stood without shoes, their heels were together with toes apart at a 60° angle, and their backs were against a calibrated backboard.

As short stature is defined as height below the 3rd centile compared to children in the same age, gender, and ethnic population¹³. In this study, China's age- and gender-specific height growth charts were used for short stature assessment¹⁴.

Statistical analysis

The demographic disparities of short stature were presented as number (percent). Prevalence was age-standardized directly to China 2010 Census. Direct standardization was conducted among provinces/municipalities/autonomous regions to make comparisons of short stature across regions easier to interpret; Chi-square test was conducted to assess differences in short stature prevalence among genders, age groups, urban/rural areas, developed/intermediately developed/under-developed regions. Cochran-Armitage test were used for trend test. Moran's I, Getis-Ord Gi*, Anselin Local Moran's I were performed to identify spatial disparities which were displayed on maps. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC) and geographical disparities were analyzed by ArcMap software 10.6. P values less than 0.05 (two-sided) were considered to be statistically significant.

Results

Characteristics of participating children

Totally, 213795 children were enrolled into our study, including 106857 boys and 106938 girls. The samples were distributed evenly among sex (the ratio of boys and girls was closed to 1:1), age, urban-rural areas, and economic development(Table.1).

Variables	N (%)		
v ariables	Boys (n= 106857)	Girls (n= 106938)	Both (n= 213795)
Age			
7	8944 (8.37)	8942 (8.36)	17886 (8.37)
8	8903 (8.33)	8929 (8.35)	17832 (8.34)
9	8962 (8.39)	8980 (8.40)	17942 (8.39)
10	8972 (8.40)	8967 (8.39)	17939 (8.39)
11	8982 (8.41)	8937 (8.36)	17919 (8.38)
12	8953 (8.38)	8951 (8.37)	17904 (8.37)
13	8968 (8.39)	8982 (8.40)	17950 (8.40)

Table 1. Characteristics of participating children in national survey in 2014

14	8964 (8.39)	8969 (8.39)	17933 (8.39)
15	8973 (8.40)	8987 (8.40)	17960 (8.40)
16	8960 (8.39)	8967 (8.39)	17927 (8.39)
17	8952 (8.38)	8980 (8.40)	17932 (8.39)
18	8324 (7.79)	8347 (7.81)	16671 (7.80)
Residence			
urban	53502 (50.07)	53537 (50.06)	107039 (50.07)
rural	53355 (49.93)	53401 (49.94)	106756 (49.93)
Economic development			
developed	35567 (33.28)	35704 (33.39)	71271 (33.34)
Intermediately	35659 (33.37)	35620 (33.31)	71279 (33.34)
developed			
under-developed	35631 (33.34)	35614 (33.30)	71245 (33.32)

Prevalence of short stature

The nation-wide prevalence of short stature was 3.67% according to China growth reference. The age-standardized prevalence of short stature nationwide were 3.70%. Based on China growth reference, the short stature prevalence differed greatly among age groups, urban-rural areas, and regions with different economic development (all p<0.0001), especially in areas (2.23% in urban vs 5.12% in rural areas, p<0.001) and regions (2.60 in developed, 3.72% in intermediately developed, 4.69% in under-developed regions, p<0.0001) (Table 2,Figure.1 A).

There are a gender statistically differences in year groups of $10\sim12,13\sim15,16\sim18$. In $10\sim12$ and $16\sim18$ year groups, the prevalence of girls is higher than boys, however in $13\sim15$ years group boys' is higher than girls' (Figure 1 B).

Table 2. Prevalence of short stature in boys and girls according to China growth

reference

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		Prevalence, %		
Stratification	Both	Boys	Girls	
China guideline/standard				
Age group				
7-9	1646 (3.07)	843 (3.14)	803 (2.99)	
10-12	1878 (3.49)	867 (3.22)	1011 (3.76)	
13-15	2396 (4.45)	1387 (5.16)	1009 (3.75)	
16-18	1927 (3.67)	874 (3.33)	1053 (4.00)	
P for trends	< 0.0001	< 0.0001	< 0.0001	
Residence				
urban	2382 (2.23)	1189 (2.22)	1193 (2.23)	
rural	5465 (5.12)	2782 (5.21)	2683 (5.02)	
P-value for difference	< 0.0001	< 0.0001	< 0.0001	
Economic development				
developed	1851 (2.60)	928 (2.61)	923 (2.59)	
Intermediately developed	2652 (3.72)	1341 (3.76)	1311 (3.68)	
under-developed	3344 (4.69)	1702 (4.78)	1642 (4.61)	
P for trends	< 0.0001	< 0.0001	< 0.0001	
total	7847(3.67)	3971 (3.72)	3876(3.62)	

Spatial characteristics of short stature

The spatial distribution of short stature prevalence exhibited a clustered pattern. Moran's I value was 0.474(P < 0.001). The short stature prevalence maps (Figure.2, Table. S1) demonstrated that the prevalence distribution was spatially heterogeneous across the study areas. Southwest China showed higher short stature prevalence while Northeast China had comparatively lower prevalence. Anselin Local Moran I indicated that there was a High-High Cluster in Sichuan, Guizhou, Guangxi, Guangdong, Chongqing, Hainan, Hunan, and Yunnan. Low-low Cluster existed in some other provinces like Liaoning, Jiling, Inner Mongolia, Beijing, Tianjin, Hebei, Shaanxi, Shandong, Jiangsu, Shanghai, Zhejiang, and Anhui (Figure.3). Getis-Ord, Gi* identified hotspot-99% confidence areas: Sichuan, Yunnan, Guizhou, Guangxi, Hainan; Hotspot-95% confidence areas: Chongqing,

Hunan, Guangdong; Hotspot-90% confidence areas: Gansu; Coldspot -99% confidence areas; Liaoning, Beijing, Tianjing, Hebei, Shandong, Shanghai, Jiangsu; Coldspot -95% confidence areas: Zhejiang, Anhui, Jiling, Inner Mongolia, Shaanxi (Figure.4). Short stature prevalence did not differ significantly among the various methods, offering a high level of confidence to this distribution pattern.

Discussion

In the present study, the national prevalence of short stature among Chinese schoolchildren aged 7-18 years was 3.67% according to China child growth standard and the age-standardized rate was 3.70%. Regarding the terminology of short stature, it sometimes equals to 'Stunted growth' which is also known as stunting and nutritional stunting. According to WHO, stunting is defined as "height for age" value of less than two standard deviations of the WHO Child Growth Standards median¹⁵. In China, definition of short stature is the height or length below the 3^{rd} centile (-1.88 SDS) or <-2SDS compared to children of the same age, gender, population¹³. Therefore, stunting prevalence can reflect the status quo of short stature epidemic in population to some extent. Globally, prevalence of stunting declined from 32.6% to 22.2% between 2000 and 2017⁹. A national survey conducted in Chinese school children in 2005 showed that 2.29% of 7-18 year-old children were stunted based on China standard¹¹. Using the same growth standard, prevalence of short stature in our study was higher than the stunting rate reported by Cai, etc almost one decade ago¹¹. This upgoing trend could be partly attributed to the different SDS adopted in our study and previous ones. In the present study, we used the 3rd centile (-1.88 SDS) to define short stature, which is routine clinic practice in China nowadays. The 3rd centile can reflect the real world of short stature diagnosis and treatment in China. In previous studies¹¹, -2 SDS was used to assess stunting, which would result in less diagnoses and lower prevalence compared to ours.

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The discrepancy between urban-rural and different economic developmental places

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Specifically, the prevalence was considerably higher in rural areas than that in urban ones. The former was nearly 2.5 times the latter one. In respect to regions with different developments, we observed a climbing trend of short stature in under-/intermediately developed regions than developed ones. Both the higher prevalence in rural areas and less developed regions indicated that children living in economically lagged-behind areas were at higher risk of being stunted growth.Based on the WHO growth reference of 2007, the stunted prevalence for children and adolescents in 2002 was 16.4% in rural China, but 5.7% in urban China¹⁶. China has made tremendous economic achievements, but this economic development does not necessarily reduce inequalities of nutrition, and health care services¹⁷.Researchers shows that there is a declining trends of urban–rural disparities since China's Reform and Opening Policy in 1978¹⁸, but the difference of prevalence of short stature in rural and urban still need to concern. This inequality remind us the policies need to implement in these area.

The discrepancy between age groups and gender

Our researcher shows difference prevalence between age groups, it maybe mainly because of the increase of height in human being is not linearly, when children step into puberty, there is growth acceleration, we also call it adolescent growth spurt. Previous studies shows the age at menarche in Chinese girls is 12.47 years in 2010^{19} . The median age of onset of puberty (testicular volume is 4 mL or greater) in urban Chinese boys was 10.55 years between 2003 and 2005^{20} . In our study, the prevalence of girls is higher than boys in $10\sim12$ and $16\sim18$ age groups, however in $13\sim15$ age group boys is higher than girl, it can explain partly by the girls' puberty earlier than boys'²¹, partly by the phenomenon than we have observe in clinical practise, that is before the adolescent growth spurt, there is a period that children's growth speed will slowdown, we can regard as a buffer stage. It remain us that the diagnose of short stature should prudent for children in this period.

Spatial characteristics of short stature

In spatial distribution, short stature prevalence was higher in southwest of China but greatly lower in northeast of China. The provinces/municipalities/autonomous regions with high short stature prevalence were mainly clustered in Southwest areas. There is a long history of drawing a spatial map basing on healthy data. In 1854, John snow draw a cholera map to find out the relationship between cholera and unclean drinking waters. Drawing a spatial map of disease prevalence can help to find out the regulation of disease take intervention and prevent the occur of disease. Previous studies showed that there is a spatial distribution of stunting. A research from Somalia shows there is a high rate of stunting in south area especially around the twomain rivers of Juba and Shebelle⁷. There is a study in Ethiopia shows that they identified statistically significant clusters of high prevalence of stunting (hotspots) in the eastern part of the district and clusters of low prevalence (cold spots) in the western⁸. In our study, we use Moran's I,Getis-Ord Gi*,Anselin Local Moran's I to explore the spatial distribution pattern of short stature, they are widely used in exploring the space-time pattern of disease. Our researcher shows that there is a significant difference in the prevalence of short stature in differences areas of China. There is a high incidence of short stature in southwestern region, especially in Sichuan, Guizhou, Guangxi, Chongging, Hainan, Yunnan provinces, the GRP(gross regional production) of these place were lag behind relatively of the rest of the China. Even though socio-economic factors maybe a crucial reason of regional disparity in prevalence of the short stature in China, the special geographic and climate features in these places we still need to notice. These places belonging subtropical monsoon climate and tropical monsoon climate, the latitude, altitude, terrain of these places are vary considerably with other parts of China. Some previous studies showed that, in mainland China, children in North had higher height than children in South on average¹¹, however, our research shows the prevalence of short stature has coincident trend with the body height, these children who live in hotpot area (some places of southwestern China) will diagnosed with short stature but they are may not pathological condition, the

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prevalence of short stature will be overstate. All of we known that Peruvians are among the world's shortest people²², Peruvians lived at high altitudes place, studies show that animals living in high elevations places tend to be smaller, because they need to adapt harsh environment where scarcity of food in high elevations places. Organisms are constantly adapting the changes of nature environment.In a word,not only socio-economic factors, but also nature environmental factor lead to the spatial difference of the prevalence of short stature in China. It hints us about except to consider racial factor, but also note regional factor when we define short stature. Further researches are

Conclusions

needed.

There is a significant highly prevalence of short stature in rural, intermediately developed, under-developed areas of China, this would provide corroborating evidence for tailored strategy on short stature prevention and reduction in special areas. We also uncover that there is spatial clusters of short stature in the southwestern China, therefore further study needs to be done in these places to detected the cause of short stature. It indicates that except for racial factor, the regional factor maybe be need to considered when we define short stature.

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Contributors

Zhang Zhixin and Ma Jun worked together to develop the research question, study design and analytic plan. Dong Yanhui and Yang Zhaogeng collected and collated data of short stature prevalence in different genders, regions, ages groups from MCNSSCH data.Ma Jia wrote the manuscript. Dong Fen analyzed demographic characteristics of data by mathematical statistics and revised the manuscript. Pei Tao, Chen Jie, Guo Sihui

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analyzed spatial distribution of short stature and Pei Tao help to revised the manuscript. Zhao Qiuling and Wang shunan help to apply the research fund and check the data.All authors have contributed to the work and approved the manuscript.

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Competing interests None declared.

Ethics approval

Informed consent was obtained from both parents and students before they participated in the study. The project was approved by the Medical Research Ethics Committee of Peking University Health Science Center (IRB00001052–13082),Clinical research ethics committee of China-Japan friendship hospital(2018-93-K67)

Data sharing statement No additional data are available.

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Fig.1 A.The discrepancy of prevalence between urban-rural and different economic developmental places.B.The discrepancy of prevalence between different age groups in boys and girls.In

10~12,13~15,16~18 year groups the difference are statistically significant(P=0.001,P<0.0001,P<0.0001

respectively, they were analyzed by chi-square test).

127x153mm (300 x 300 DPI)





Fig.2 The distribution of short stature standardized prevalence in China (2014)

206x207mm (300 x 300 DPI)





Fig.3 The results of Anselin Local Moran's I about short stature in China (2014)

206x207mm (300 x 300 DPI)

Fig.4 The result of Hotspot Getis-Ord, Gi about short stature in China (2014)

206x207mm (300 x 300 DPI)

Supplementary

Table S1. The prevalence and standardize prevalence of short stature in provinces

Province	China refer	China reference		
	N(%)	Age-standardized rate, %		
Beijing	0.62	0.58		
Tianjin	0.75	0.77		
Hebei	1.29	1.3		
Shanxi	3.08	3.14		
Inner Mongolia	1.9	1.91		
Liaoning	1.1	1.1		
Jilin	1.81	1.82		
Heilongjiang	2.86	2.8		
Shanghai	0.84	0.82		
Jiangsu	0.72	0.74		
Zhejiang	1.3	1.3		
Anhui	2.1	2.1		
Fujian	1.13	1.14		
Jiangxi	4	4.06		
Shandong	0.42	0.42		
Henan	1.76	1.79		
Hubei	2.53	2.59		
Hunan	4.8	4.82		
Guangdong	4.93	4.95		
Guangxi	6.84	6.86		
Hainan	7.49	7.4		
Chongqing	7.25	7.37		
Sichuan	8.61	8.66		
Guizhou	13.51	13.61		
Yunnan	4.68	4.64		
Shaanxi	6.32	6.46		
Gansu	3.39	3.49		
Qinghai	6.2	6.31		
Ningxia	3.42	3.45		

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Spatial and Demographic Disparities in Short Stature among Schoolchildren aged 7-18 years: a Nation-wide Survey in China, 2014

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Primary Subject Heading :	Paediatrics
Secondary Subject Heading:	Diabetes and endocrinology, Public health
Keywords:	short stature, prevalence, China, spatial disparities, demographic disparities

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1		Spatial and Demographic Disparities in Short Stature among
2	Sc	chool Children Aged 7-18 Years: A Nation-Wide Survey in China,
3		2014
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Abstract **Objectives:** To identifying spatial disparities and demographic characteristics of short stature, we analyzed the prevalence of short stature collected in a nationwide health survey. **Settings:** Data were obtained from the 2014 CNSSCH (a cross-sectional study of China). The students came from 30 provinces, autonomous regions, and municipalities (except Tibet, Hong Kong, Macao, and Taiwan). **Participants:** There were 213,795 Han students between 7–18 years old enrolled in our study. All participants were sampled by stratified cluster. Primary and secondary outcome measures: Short stature; Chinese and WHO age- and gender-specific height growth references were used for short stature assessment. **Results:** The age-standardized and age-gender-standardized prevalence of short stature nationwide were 3.70 and 2.69% according to Chinese and WHO growth references, respectively. The short stature prevalence differed significantly among age groups, urban and rural areas, and regions with different socioeconomic development levels (all p < p0.0001). The prevalence was 2.23% in urban versus 5.12% in rural areas (p < 0.001). The prevalence was 2.60% in developed, 3.72% in intermediately-developed, and 4.69% in under-developed regions (p < 0.0001). This was all according to China's growth reference, but similar patterns were observed on prevalence based on the WHO reference. The spatial distribution of short stature prevalence exhibited a clustered pattern. Moran's I value was 0.474 (p < 0.001) and 0.478 (p < 0.001) according to the Chinese and WHO growth references, respectively. The southwest part of China showed a higher short stature prevalence, whereas lower short stature prevalence was observed mainly in the northeast part of China. **Conclusions:** There is an appreciably high prevalence of short stature in rural, under-developed areas of China. We also uncovered that there are spatial clusters of

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4	1	short stature in southwestern China. This provides corroborating evidence for a tailored
5 6	2	strategy on short stature prevention and reduction in special areas.
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13 14	6	Strengths and Limitations of This Study
15 16	7	This is the first study to detect the spatial discrepancy of short stature prevalence in
17 18	8	mainland China.
19 20	9	The results provide corroborating evidence for a tailored strategy on short stature
21 22	10	prevention and reduction in special areas.
23 24	11	Our study raises a discussion that, because of the geographical and climatic
25 26	12	differences between north and south China, we may need to consider regional differences
27 28	13	in height when we diagnose short stature.
29 30	14	Our study is a cross-sectional study. We did not explore the cause of short stature
31 32	15	and did not perform a follow-up to learn the adult heights of our participants.
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1 Introduction

Short stature is a major morbid condition for children who are referred to pediatric endocrinologists.¹⁻³ About half of new visits to the pediatric endocrine department are harassed by short stature.⁴ It is usually caused by multiple factors, including children's nutritional status, repeated infections due to unsanitary environmental conditions, and the existence of several unknown endocrine metabolic disorders.⁵ The causes of short stature are a wide spectrum and mainly divided into normal (e.g., familial short stature and constitutional delay of growth) and pathological (e.g., growth hormone deficiency, Turner syndrome, hypothyroidism, chronic diseases, idiopathic short stature, etc.).⁶ It is regrettable that some of the causes of this morbid status remained unidentified; we call this idiopathic short stature. With the advancement of molecular diagnostic techniques, some unexplained causes for short stature have been gradually revealed. It can somewhat be attributed to genetic variation, indicating short stature as a phenotype of genetic diseases.⁴ Additionally, short stature affects children's physical and mental health. Children with short stature tend to suffer psychological disorders, such as low self-esteem, depression, social immaturity, behavioral problems, and academic difficulties.⁷ Short stature can still affect children's health after they grow up. For instance, females with short stature were susceptible to have preterm birth when they became pregnant in adulthood.⁸ Therefore, identifying short stature in childhood is extremely important for physical and mental illness reduction and should be an imperative part of children's health programs.

The prevalence of short stature varies greatly among different regions due to diverse social development and natural environment.⁹⁻¹² It has been reported that children living in undeveloped areas were more likely to have stunted growth (or short stature). In 2017, the United Nations International Children's Emergency Fund data showed that the prevalence of stunting in children under five years old in East and South Africa and South Asia were 34.1 and 35%, respectively.¹³ Another study showed that children in

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north China were taller, on average, than children in south China. ¹⁴ In addition, children
living in economically developed areas such as Hong Kong (which located in the south of
China) were also susceptible to a certain percentage of short stature, indicating that there
are other reasons that cause short stature. ¹⁵ For example, geographical-climate factors
may play an important role in short stature. Is there a special spatial distribution of short
stature in mainland China? Is this distribution associated with socioeconomic or
geographical characteristics? Unfortunately, data related to the geographical distribution
of short stature in China is seldom reported. To fill such a gap, we analyzed the
schoolchildren's height in a nationwide health survey, aiming to identify the spatial
disparities and demographic characteristics of short stature.
Methods
Date Collection and Sampling
Data were collected from the 2014 Chinese National Survey on Students
Constitution and Health (CNSSCH), a national health survey on schoolchildren. Eligible
participants were Han Chinese individuals aged 7–18 years old. The sampling procedures
of CNSSCH have been published. ¹⁶ In summary, all participants were collected by
stratified cluster sampling according to the principle of CNSSCH. Selected places in each
province were graded into developed, intermediately-developed, under-developed levels
based on the local socioeconomic development. Subsequently, children were divided into
four strata: urban boys, urban girls, rural boys, and rural girls. Then, 50 people were
collected in each unit (for each year of age, gender, the urban/rural,
developed/intermediately-developed/under-developed groups, and province). In the end,
213,795 Han students were enrolled in our study, and they came from 30 provinces,
autonomous regions, or municipalities (except Tibet, Hong Kong, Macao, and Taiwan).
The 18-year-old schoolchildren of Beijing could not be divided into three classes based
on the condition of socioeconomic development, so we excluded the data of this group.
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China) were also susceptible to a certain perc are other reasons that cause short stature.¹⁵ Fo may play an important role in short stature. Is stature in mainland China? Is this distribution geographical characteristics? Unfortunately, of short stature in China is seldom reported. schoolchildren's height in a nationwide health disparities and demographic characteristics of **Methods** Date Collection and Sampling Data were collected from the 2014 Chin Constitution and Health (CNSSCH), a nation participants were Han Chinese individuals ag of CNSSCH have been published.¹⁶ In summ stratified cluster sampling according to the pr province were graded into developed, interme based on the local socioeconomic developme four strata: urban boys, urban girls, rural boys collected in each unit (for each year of age, g developed/intermediately-developed/under-213,795 Han students were enrolled in our stu autonomous regions, or municipalities (excep The 18-year-old schoolchildren of Beijing co on the condition of socioeconomic developme e For peer review only - http://bmjopen

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This study, approved by six ministries of China, was conducted in accordance with the guidelines laid down in the Declaration of Helsinki. We obtained informed consent from parents and students. This study was approved by the Medical Research Ethics Committee of Peking University Health Science Center (IRB00001052-13082) and the clinical research ethics committee of the China–Japan friendship hospital(2018-94-K68).

6 Anthropometric Measurements

Standing height (cm) was measured by trained staff following a standardized procedure, which followed with the anthropometry methods in the 2006 World Health Organization (WHO) Child Growth Standards.¹⁷ Height was measured to the nearest 0.1 cm with portable stadiometers. Children stood without shoes, their heels were together with toes apart at a 60° angle, and their backs were against a calibrated backboard. Short stature is defined as a height below the 3rd centile compared to children in the same age, gender, and ethnic population.¹⁸ In this study, we used China's and WHO's age- and gender-specific height growth references for short stature assessment.¹⁹

15 Statistical Analysis

The demographic disparities of short stature were presented as a number (percent). Prevalence was age-standardized (i.e., age-gender-standardized) directly to the China 2010 Census. Direct standardization was conducted among provinces, municipalities, and autonomous regions to make comparisons of short stature across regions easier to interpret. The Chi-square test was conducted to assess differences in short stature prevalence among genders, age groups, urban/rural areas, and regions of different developmental levels. The Cochran–Armitage test was used for testing trend. Moran's I, Getis-Ord Gi*, and Anselin Local Moran's I were performed to identify spatial disparities. Getis-Ord Gi* and Anselin Local Moran's I results were displayed on maps. Moran's I is a measure of spatial autocorrelation developed by Patrick Alfred Pierce Moran in 1950.^{20, 21} Moran's I ranges from -1 to 1. Values close to zero indicate the absence of a spatial association (i.e., a random distribution), values close to negative one

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		(n = 106857)	(n = 106938)	(n = 213795
	Variables	Boys	Girls	Both
			N (%)	
23 24	Table 1 Characteristics of particular	rticipating children i	n the national su	rvey in 2014
22	and regions with different socioe	conomic development	t levels (Table 1).	
21	boys and girls was close to 1:1) and among the groups of different ages, urban-rural area			
20	in our study. The participants were distributed evenly between sexes (i.e., the ratio of			
19	In total, 213,795 children, comprising 106,857 boys and 106,938 girls, were enrolled			
18	Characteristics of Participating Children			
17	Results			
16				
15	Participants were not involved in the design of this study.			
14	Patient and Public Involvement			
13	than 0.05 (two-sided) were considered statistically significant.			
12	analyzed by ArcMap software 10.2 (ESRI, Redlands, California, USA). p-values less			
11	using SAS version 9.4 (SAS Institute Inc, Cary, NC) and geographical disparities were			
10	mixed clustering (i.e., low near high or vice versa). Statistical analyses were performed			
9	Moran's I to estimate the spatial clustering of high-high clustering, low-low clustering, or			
8	specified geographical area (inter	c-cluster variation). ²³	We used the Ansel	in Local
7	estimates the association of the sl	hort stature cluster and	l its neighboring c	lusters within
6	suggest lower short stature clustering. Local Moran's I, proposed by Luc Anselin in 199:			
5	stature clustering, scores near 0 indicate no clustering existed, and negative scores			
4	Keith Ord in 1992 ²² In our study more highly positive Gi * Z-scores indicate high shor			
2	considered statistically significant. Getis-Ord Gi* was proposed by Arthur Getis and			
2	clustering (autocorrelation) Mor	an's I statistics with n	-values less than 0	05 are

7	8944 (8.37)	8942 (8.36)	17886 (8.37)
8	8903 (8.33)	8929 (8.35)	17832 (8.34)
9	8962 (8.39)	8980 (8.40)	17942 (8.39)
10	8972 (8.40)	8967 (8.39)	17939 (8.39)
11	8982 (8.41)	8937 (8.36)	17919 (8.38)
12	8953 (8.38)	8951 (8.37)	17904 (8.37)
13	8968 (8.39)	8982 (8.40)	17950 (8.40)
14	8964 (8.39)	8969 (8.39)	17933 (8.39)
15	8973 (8.40)	8987 (8.40)	17960 (8.40)
16	8960 (8.39)	8967 (8.39)	17927 (8.39)
17	8952 (8.38)	8980 (8.40)	17932 (8.39)
18	8324 (7.79)	8347 (7.81)	16671 (7.80)
Residence			
Urban	53502 (50.07)	53537 (50.06)	107039 (50.07)
Rural	53355 (49.93)	53401 (49.94)	106756 (49.93)
Socioeconomic development			
Developed	35567 (33.28)	35704 (33.39)	71271 (33.34)
Intermediately developed	35659 (33.37)	35620 (33.31)	71279 (33.34)
Under-developed	35631 (33.34)	35614 (33.30)	71245 (33.32)

Prevalence of Short Stature

The nationwide prevalence of short stature was 3.67 and 2.70% according to the Chinese and WHO growth references, respectively. Based on the Chines growth reference, short stature prevalence differed significantly among age groups, urban-rural areas, and regions with different socioeconomic development levels (all p < 0.0001). This was especially true for urban versus rural areas (i.e., 2.23 vs 5.12%, respectively; p <

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0.0001) and regions of varying socioeconomic development (i.e., 2.60 in developed, 3.72% in intermediately-developed, and 4.69% in under-developed regions; p < 0.0001) (Table 2 and Figure 1A). Similar patterns were observed in the short stature prevalence based on the WHO reference (Table 2 and Figure 1A). The age-standardized and age-gender-standardized prevalence of short stature nationwide were 3.70 and 2.69% according to the Chinese and WHO growth standards, respectively. Notedly, the prevalence of short stature defined by the Chinese standard was higher than that based on the WHO standard.

10 Table 2 Prevalence of short stature in boys and girls according to China and

11 WHO references

St			
Stratification	Both	Boys	Girls
	China guideline/sta	ndard	
Age group (years)			
7-9	1646 (3.07)	843 (3.14)	803 (2.99)
10-12	1878 (3.49)	867 (3.22)	1011 (3.76)
13-15	2396 (4.45)	1387 (5.16)	1009 (3.75)
16-18	1927 (3.67)	874 (3.33)	1053 (4.00)
P for trends	< 0.0001	< 0.0001	< 0.0001
Residence			
Urban	2382 (2.23)	1189 (2.22)	1193 (2.23)
Rural	5465 (5.12)	2782 (5.21)	2683 (5.02)
P-value for difference	< 0.0001	< 0.0001	< 0.0001
Socioeconomic development			
Developed	1851 (2.60)	928 (2.61)	923 (2.59)
Intermediately developed	2652 (3.72)	1341 (3.76)	1311 (3.68)
Under-developed	3344 (4.69)	1702 (4.78)	1642 (4.61)
P for trends	< 0.0001	< 0.0001	< 0.0001
Total	7847 (3.67)	3971 (3.72)	3876 (3.62)

Age group (years)

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5780 (2.7)	2365.00 (2.21)	3415 (3.19)
< 0.0001	< 0.0001	< 0.0001
2424 (3.40)	995 (2.79)	1429 (4.01)
1979 (2.78)	821 (2.30)	1158 (3.25)
1377 (1.93)	549 (1.54)	828 (2.32)
< 0.0001	< 0.0001	< 0.0001
3957 (3.71)	1611 (3.02)	2346 (4.39)
1823 (1.70)	754 (1.41)	1069 (2.00)
< 0.0001	< 0.0001	< 0.0001
2485 (4.73)	1152 (4.39)	1333 (5.07)
1525 (2.83)	718 (2.67)	807 (3.00)
994 (1.85)	164 (0.61)	830 (3.09)
776 (1.45)	331 (1.23)	445 (1.66)
	776 (1.45) 994 (1.85) 1525 (2.83) 2485 (4.73) <0.0001 1823 (1.70) 3957 (3.71) <0.0001 1377 (1.93) 1979 (2.78) 2424 (3.40) <0.0001	776 (1.45) $331 (1.23)$ $994 (1.85)$ $164 (0.61)$ $1525 (2.83)$ $718 (2.67)$ $2485 (4.73)$ $1152 (4.39)$ <0.0001 <0.0001 $1823 (1.70)$ $754 (1.41)$ $3957 (3.71)$ $1611 (3.02)$ <0.0001 <0.0001 $1377 (1.93)$ $549 (1.54)$ $1979 (2.78)$ $821 (2.30)$ $2424 (3.40)$ $995 (2.79)$ <0.0001 <0.0001

We did not observe a gender difference in overall short stature prevalence according to the Chinese growth reference (p = 0.260). However, we captured this difference in prevalence evaluated by the WHO growth reference (p < 0.0001). Because we found significant differences of short stature prevalence in urban and rural areas and regions with different socioeconomic development levels, we then explored further to see if a gender difference of short stature existed in different areas and regions. Based on the Chinese reference, results (Table 3) showed that there are no significant differences in short stature prevalence between genders in urban or rural areas or in regions of different socioeconomic development levels. According to the WHO reference, there are significant differences in gender between urban or rural areas and among all the regions of different socioeconomic development levels.

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	χ^2	p value	χ^2	p value
Residence				
Urban	0.004	0.947	55.163	< 0.0001
Rural	1.981	0.159	141.122	< 0.0001
Socioeconomic development				
Developed	0.041	0.840	56.555	< 0.0001
Intermediately developed	0.319	0.572	59.406	< 0.0001
Under-developed	1.100	0.294	80.656	< 0.0001
Total	1.270	0.260	195.227	<0.0001

Then, we drew trajectories of short stature prevalence across different ages for boys and girls in different areas of residence (urban/rural) and regions (i.e., developed, intermediately-developed, or under-developed) (Figure 1B and C, and Supplementary Figure.1). The high prevalence of short stature in rural or undeveloped regions are consistent across all ages. In addition, we had two interesting findings that applied to all children no matter whether they lived in urban or rural areas or regions of different socioeconomic development levels. The first is that, in most cases, although the trajectories of short stature prevalence in different age groups fluctuated, and the lowest point was always in the 10-12 age group for boys and the 7-9 age group in girls. The second finding is that, in most cases, the peak of short stature prevalence appeared after the lowest point. Some of them followed closely in the next age group while others appeared in the 16–18 age group.

Spatial Characteristics of Short Stature

The spatial distribution of short stature prevalence exhibited a clustered pattern. Moran's I value was 0.474 (p < 0.001) and 0.478 (p < 0.001) according to the Chinese and WHO growth references, respectively. The short stature prevalence maps (Figures 2A, 2B and Supplementary Table 1) demonstrated that the prevalence distribution was spatially heterogeneous across the study areas. Southwest China showed higher short

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stature prevalence while northeast China had comparatively lower prevalence. Anselin Local Moran I indicated that there was a high-high cluster in Sichuan, Guizhou, Guangxi, Guangdong, Chongqing, Hainan, Hunan, and Yunnan. A low-low cluster existed in some other provinces like Liaoning, Jiling, Inner Mongolia, Beijing, Tianjin, Hebei, Shaanxi, Shandong, Jiangsu, Shanghai, Zhejiang, and Anhui (Figures 2C, 2D and Supplementary Table 2). These results were consistent between the two references. According to the Chinese growth reference, Getis-Ord Gi* identified the following as hotspot-99% confidence areas: Sichuan, Yunnan, Guizhou, Guangxi, and Hainan. The hotspot-95% confidence areas were Chongqing, Hunan, and Guangdong. The hotspot-90% confidence area was Gansu. The coldspot-99% confidence areas were Liaoning, Beijing, Tianjing, Hebei, Shandong, Shanghai, and Jiangsu. The coldspot-95% confidence areas were Zhejiang, Anhui, Jiling, Inner Mongolia, and Shanxi (Figure 2E and Supplementary Table 3). According to the WHO growth reference, Getis-Ord Gi* identified the following hotspot-99% confidence areas: Sichuan, Yunnan, Guizhou, Guangxi, and Hainan. The hotspot-95% confidence areas were Chongqing, Hunan, and Guangdong. The coldspot-99% confidence areas were Liaoning, Beijing, Tianjing, Hebei, Shandong, Shanghai, and Jiangsu. The coldspot-95% confidence areas were Anhui, Jiling, Inner Mongolia, and Shanxi. The coldspot-90% confidence areas was Zhejiang (Figure 2F Supplementary Table 3). Short stature prevalence did not differ significantly among the various methods, offering a high level of confidence to this distribution pattern.

22 Discussion

In our study, the age-standardized and age-gender-standardized prevalence of short stature nationwide were 3.70 and 2.69% according to Chinese and WHO growth standards, respectively. Regarding the terminology of short stature, it is sometimes synonymous to "stunted growth" and also known as stunting or nutritional stunting in children. According to WHO, stunting is defined as a "height-for-age" value of less than

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two Standard Deviations Score (SDS) of the WHO Child Growth Standards median.²⁴ In China, the definition of short stature is a height-for-age below the third centile (-1.88)SDS) or less than 2 SDS compared to average height children of the same age, gender.¹⁸ Globally, the prevalence of stunting under five years old declined from 32.6 to 22.2% between 2000 to 2017.¹³ One study in 2014 showed that the crude prevalence of stunting in Chinese schoolchildren between 7–18 years old was 2.3% based on the WHO growth reference, which is lower than our result.²⁵ This difference could be partly attributed to the different SDS adopted in our study. We used the third centile (-1.88 SDS) to define short stature, which is currently routine clinical practice in China. In Song's study, -2SDS was used to assess stunting, which resulted in less diagnoses and a lower prevalence compared to our study. Their study also showed that, from 1985 to 2014, the national crude prevalence of stunting in Chinese schoolchildren decreased from 16.4 to 2.3%.²⁵ Another study in Hong Kong processed in 2005 showed that the crude prevalence of short stature (i.e., height below the third centile) was 1.7% in 6–10 year-old children and was 4.4% in 11–18 year-olds based on the WHO growth reference. World Bank data showed that the prevalence of stunting in 2015 among children under 5 years old in South Asia, Sub-Saharan Africa, the Middle East and North Africa, East Asia and the Pacific, Latin America and the Caribbean, and Europe and Central Asia were 36.2, 35.2, 15.8, 14.4, 10.1, and 9.2%, respectively.²⁶ In conclusion, the total prevalence of short stature among Chinese schoolchildren being low and having a decreased trend may reflect improvements in many aspects of China in recent years.²⁵ The prevalence of short stature helps us to know the nutritional and pathological condition of children and provide healthy data to decision makers. The prevalence of short stature was considerably higher in rural areas than in urban

The prevalence of short stature was considerably higher in rural areas than in urban ones. The prevalence in the former was nearly 2.5 times higher than in the latter. With respect to regions with different socioeconomic development levels, we observed a climbing trend of short stature in under- and intermediately-developed regions compared

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1	to developed ones. Both the higher prevalence in rural areas and less developed regions
2	indicated that children living in socioeconomically delayed areas were at a higher risk of
3	having stunted growth. Based on the WHO growth reference of 2007, the prevalence for
4	stunted children and adolescents in 2002 was 16.4% in rural China and 5.7% in urban
5	China. ²⁷ China has made tremendous economic achievements, but this economic
6	development does not necessarily reduce inequalities in nutrition and health care
7	services. ²⁸ A study has shown that there have been declining trends of urban-rural
8	disparities since China's Reform and Opening Policy was established in 1978.29 However,
9	the difference in the prevalence of short stature in rural and urban areas is still a concern.
10	This inequality reminds us of the need for policies to be implemented in this area.
11	Our study has shown differences in prevalence between age groups. These differences
12	may be mainly because the increase of height in human beings does not occur at a
13	constant velocity. The highest growth rate occurs in fetal life and infancy, then slows
14	down during childhood before accelerating during puberty. ^{30, 31} The acceleration of the
15	rate of height growth in puberty can partly explain the differences in short stature
16	prevalence between in different age groups. When does puberty begin in Chinese
17	adolescents? Girls may begin puberty earlier than boys. ³² One study showed that the
18	median age of menarche in Chinese girls was 12.47 years in 2010. ³³ Puberty starts almost
19	two years before the age of menarche in girls. The median age of puberty onset (i.e.,
20	testicular volume is 4 mL or greater) in urban Chinese boys was 10.55 years between
21	2003 and 2005. ³⁴ Another study showed the menarche of Hong Kong Chinese girls
22	occurred at 12.1 years, and the first nocturnal ejaculation occurred at 13.0 years for Hong
23	Kong Chinese boys in 1996. ³⁵ The timing of puberty reported by literature is consistent
24	with our study results. The lowest point of short stature prevalence occurred in the 10–12
25	and 7–9 age groups for boys and girls, respectively. During these ages, Chinese boys and
26	girls start puberty. The rate of height growth accelerated, whereas short stature
27	prevalence lowered correspondingly. The phenomena of the peak appearing after the

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lowest point may indicate that, after puberty, the growth rate gradually decreased in these age groups, especially in the 16–18 age group. One study showed that most Chinese children will stop height growth by the time they reach 18 years of age.¹⁹ On account of these changes in the height growth rate during puberty, the diagnosis of short stature may be prudent for children between 7 and 18 years old.

As for gender differences in short stature prevalence, the two growth references gave opposite results. We found that, in the 10-12 age group, the prevalence of short stature in boys based on the WHO reference was unusually low at 0.61% (Figure 2). We think that the reason behind this is related to the acceleration of puberty in Chinese boys of this age group and to the fact that the data of the WHO reference did not detect boys who are really short stature. Two studies in Argentinian and Polish children showed growth variations, especially in adolescents, when comparing the WHO growth reference data with the recommend national references for clinical use.^{36, 37} Another study showed that Asian subpopulations have an earlier onset of puberty than other ethnic groups.³⁸ In conclusion, using US children pubertal growth patterns (i.e., WHO reference for 5–19 vears based on the data of the US population) to assess Chinese children pubertal growth patterns may be inappropriate. We recommend the use of the Chinese growth reference for clinical assessment.

In terms of spatial distribution, our study showed that short stature prevalence was higher in southwest of China but lower in northeast China. With the development of the geographic information system (GIS) technique, the research on the spatial distribution for diseases has gradually attracted people's attention.³⁹⁻⁴³ A study from Somalia shows that there is a high prevalence of stunting in the south area of the country, especially around the two main rivers of Juba and Shebelle.¹¹ There is a study in Ethiopia showing that they identified statistically significant clusters of high prevalence of stunting (hotspots) in the eastern part of the district and clusters of low prevalence (cold spots) in the western part of the district.¹² In our study, we tried to explore the spatial

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discrepancy of short stature in mainland China using Moran's I. Getis-Ord Gi*, and Anselin Local Moran's I, which are widely used in exploring the space-time pattern of diseases. Our research shows that there is a significant difference in the prevalence of short stature in different areas of China. Specifically, there is a higher prevalence cluster for short stature in the southwestern region, especially in the Sichuan, Guizhou, Guangxi, Guangdong, Chongqing, Hainan, and Yunnan provinces. In the northeast region, there was a lower prevalence cluster for short stature, especially in Inner Mongolia, Beijing, Tianjin, Hebei, Liaoning, Jilin, Shandong, Shanxi, Shanghai, Zhejiang, Anhui, and Jiangsu. What accounts for this spatial discrepancy? Socio-economic factors may account for something.^{44, 45} Two studies about spatial difference of stunting mentioned above found that maternal education and food security and access were associated with stunting.^{11, 12} In addition, the discrepancies in some disease conditions, such as repeated infections and endocrine metabolic disease, may affect the distribution of short stature. It is a complicated situation, and we hope we can deeply research this in future studies. Another study that caught our attention found that, in mainland China, children of 7 to 18 years old living in the north had a higher height than children in the south on average.¹⁴ The maximum height difference of different regions was almost 4 to 5 cm.¹⁴ China is not a country of immigrants. Residents have lived here for thousands of years, and residents and the natural environment have developed adaptations. Because there is a disparity in the geographic-climatic environment between south and north China, we believe that the geographic-climatic factor may play an important role in short stature. Firstly, altitudes may be an important factor for height growth and is associated with short stature. Peruvians and Tibetans lived at high altitude places and tend to be short.⁴⁶⁻⁴⁸ Because of the high altitude environment, the body's functions will exhibit high-altitude adaptations, such as larger lungs, better lung function, lower blood hemoglobin concentration, etc., that may not be found in lowlanders.⁴⁹ Short stature may be another type of adaption because animals living in high elevations tend to be smaller to adapt to

an environment with a scarcity of food.⁴⁶ Even European settlers living in the Andes had statures 1–5 cm shorter than their compatriots living in lowland areas.⁵⁰ Moreover, temperature, rainfall, and extreme weather events (floods/droughts) were reported to be associated with short stature.^{11, 51-53} Regrettably, we did not explore the causes of short stature. The geographic-climatic factor may determine short stature to some degree. Therefore, children who live in hotpot areas (some places in southwestern China) will be diagnosed with short stature though they do not have a pathological condition. The prevalence of short stature will be overestimated. The solutions for this are to build growth standards based on the same area population or lower the cut-off value to diagnose short stature in these places. We must be more prudent when we diagnose short stature of children from these areas and avoid excessive laboratory tests or therapy for these children. Further studies on this subject are needed, and we hope our study is raising a discussion on the topic.

14 Limitations

Height varies between different population groups worldwide.^{54, 55} The Dutch population is the tallest and the Peruvian population is the shortest population in the word.^{46, 56} Even immigrants will retain genetic potential for height, as observed in Turkish children.⁵⁷ The definition of short stature emphasizes that the comparison of height needs to be between the same population group, race, or ethnic minority.^{18, 58} There are 56 ethics groups (nationalities) in China, as shown by the 2011 National Population Census data. Of the Chinese population, 91.51% are of Han nationality and 8.49% are of "minority nationalities".⁵⁹ A study compared the height of minority nationalities with Han schoolchildren in southwest China. Results showed that the age of the rapid growth period in the southwest China minority nationality group was greater than that in the Han schoolchildren.⁶⁰ Another study showed that the stunting prevalence of Tibetan children in Lasa (Tibet) was higher than the national prevalence.⁶¹ Based on the above, the adult height or growth pattern of some minority nationalities may differ from the Han

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nationality in China, and it may meaningful to know the condition of short stature in
these ethnic minorities to see if it is any different to other groups (i.e., the Han nationality
or other nationalities) who live in same geographical environment. Although we did not
evaluate the short stature of ethnic minorities in our study, it is a meaningful research
direction for later scholars. In our study, we also did not exclude the effect of the floating
population (i.e., individuals whose growth place and birth place are not the same).
Because our study is cross-sectional, we also did not explore the causes of short stature
and we did not perform a follow-up to learn the adult heights of our participants.

9 Conclusions

There is an appreciably high prevalence of short stature in rural, under-developed areas of China. This provides corroborating evidence for a tailored strategy for short stature prevention and reduction in special areas. We also uncover that there is spatial clusters of short stature in the southwestern China, such as Sichuan, Guizhou, Guangxi, Guangdong, Chongqing, Hainan, Yunnan provinces. Therefore, further study needs to be done in these places to detect the cause of short stature. Our results indicate that, aside from the racial factor, the regional factor may need to be considered when defining short stature.

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Contributors

Zhixin Zhang and Jun Ma worked together to develop the research question, study
 design and analytic plan. Yanhui Dong and Zhaogeng Yang collected and collated data of

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2	Jia Ma wrote the manuscript. Fen Dong analyzed demographic characteristics of data by				
3	mathematical statistics and revised the manuscript. Tao Pei, Jie Chen, Sihui Guo analyzed				
4	spatial distribution of short stature and Tao Pei helped to revised the manuscript. Qiuling				
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Figure Legends

Figure 1

A. The discrepancy of prevalence between urban-rural and different regions.

- B. The discrepancy of prevalence between different age groups according China growth reference.
- C. The discrepancy of prevalence between different age groups according WHO growth reference.

Figure 2

- A. The distribution of short stature standardized prevalence according China growth reference.
- B. The distribution of short stature standardized prevalence according WHO growth reference.
- C. The results of Anselin Local Moran's I about short stature according China growth reference.
- D. The results of Anselin Local Moran's I about short stature according WHO growth reference.
- E. The result of Hotspot Getis-Ord, Gi* about short stature according China growth reference.
- F. The result of Hotspot Getis-Ord, Gi* about short stature according WHO growth reference.



A.The discrepancy of prevalence between urban-rural and different regions. B.The discrepancy of prevalence between different age groups according China growth reference. C.The discrepancy of prevalence between different age groups according WHO growth reference. BMJ Open: first published as 10.1136/bmjopen-2018-026634 on 16 July 2019. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.



A.The distribution of short stature standardized prevalence according China growth reference. B.The distribution of short stature standardized prevalence according WHO growth reference. C.The results of Anselin Local Moran's I about short stature according China growth reference. D.The results of Anselin Local Moran's I about short stature according WHO growth reference. E.The result of Hotspot Getis-Ord,Gi* about short stature according China growth reference. F.The result of Hotspot Getis-Ord,Gi* about short stature according WHO growth reference.

Supplementary

Table 1 The prevalence and standardize prevalence of short stature in provinces

Province	China referenc	e	WHO reference		
	N (%)	Age-standardized prevalence, %	N (%)	Age-gender standardized prevalence, %	
Beijing	41 (0.62)	0.64	22 (0.33)	0.31	
Tianjin	54 (0.75)	0.77	38 (0.53)	0.52	
Hebei	93 (1.29)	1.3	77 (1.07)	1.05	
Shanxi	222 (3.08)	3.14	152 (2.11)	2.12	
Inner Mongolia	134 (1.9)	1.91	94 (1.33)	1.31	
Liaoning	79 (1.1)	1.1	60 (0.83)	0.83	
Jilin	129 (1.81)	1.82	91 (1.28)	1.29	
Heilongjiang	205 (2.86)	2.8	134 (1.87)	1.81	
Shanghai	60 (0.84)	0.82	43 (0.6)	0.60	
Jiangsu	50 (0.72)	0.74	38 (0.55)	0.57	
Zhejiang	93 (1.3)	1.3	83 (1.16)	1.14	
Anhui	151 (2.1)	2.1	121 (1.68)	1.67	
Fujian	81 (1.13)	1.14	57 (0.79)	0.79	
Jiangxi	287 (4)	4.06	214 (2.98)	2.97	
Shandong	30 (0.42)	0.42	31 (0.43)	0.43	
Henan	127 (1.76)	1.79	93 (1.29)	1.28	
Hubei	178 (2.53)	2.59	120 (1.7)	1.75	
Hunan	345 (4.8)	4.82	281 (3.91)	3.83	
Guangdong	355 (4.93)	4.95	276 (3.83)	3.78	
Guangxi	472 (6.84)	6.86	380 (5.51)	5.43	
Hainan	539 (7.49)	7.4	403 (5.6)	5.45	
Chongqing	522 (7.25)	7.37	407 (5.65)	5.61	
Sichuan	620 (8.61)	8.66	477 (6.63)	6.52	
Guizhou	972 (13.51)	13.61	725 (10.07)	10.04	
Yunnan	337 (4.68)	4.64	247 (3.43)	3.38	
Shaanxi	454 (6.32)	6.46	320 (4.46)	4.45	
Gansu	244 (3.39)	3.49	167 (2.32)	2.34	
Qinghai	446 (6.2)	6.31	275 (3.82)	3.83	
Ningxia	235 (3.42)	3.45	158 (2.3)	2.30	
Xinjiang	292 (4.11)	4.09	196 (2.76)	2.69	

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Province	China reference			WHO reference		
	Z Score	P Value	Туре	Z Score	P Value	Туре
Zhejiang	1.99	0.008	LL	1.82	0.024	LL
Yunnan	4.23	0.002	HH Not	4.31	0.002	HH Not
Xinjiang	0.87	0.258	Significant	0.60	0.214	Significant
Sichuan	3.48	0.002	HH Not	3.71	0.002	HH Not
Shaanxi	-0.08	0.492	Significant	-0.09	0.47	Significant
Shanxi	2.37	0.008	LL	2.38	0.004	LL
Shandong	3.52	0.002	LL Not	3.36	0.002	LL Not
Qinghai	0.74	0.214	Significant Not	0.64	0.24	Significant Not
Ningxia	-0.20	0.396	Significant	0.01	0.458	Significant
Inner						
Mongolia	2.17	0.008	LL	2.18	0.004	LL
Liaoning	2.75	0.002	LL	2.67	0.002	LL
			Not			Not
Jiangxi	-0.11	0.466	Significant	0.09	0.444	Significant
Jilin	2.03	0.006	LL	1.97	0.006	LL
Hunan	2.05	0.02	HH Not	2.47	0.014	HH Not
Hubei	-0.39	0.348	Significant Not	-0.62	0.288	Significant Not
Heilongjiang	0.98	0.198	Significant Not	0.99	0.15	Significant Not
Henan	1.12	0.138	Significant	1.07	0.15	Significant
Beijing	2.04	0.002	LL	1.90	0.002	LL
Tianjin	2.27	0.002	LL	2.32	0.002	LL
Hainan	2.69	0.014	HH	3.02	0.01	HH
Guizhou	3.65	0.002	HH	3.91	0.002	HH
Guangxi	3.62	0.002	HH Not	4.12	0.002	HH Not
Gansu	-1.65	0.066	Significant Not	-1.54	0.088	Significant Not
Fujian	0.08	0.494	Significant	-0.18	0.406	Significant
Anhui	2.43	0.002	LL	2.39	0.008	LL

Table 2	The results of Anselin Local Moran's I

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Shanghai	2.52	0.002	LL	2.39	0.002	LL
Chongqing	3.23	0.002	HH	3.45	0.002	HH
Jiangsu	2.97	0.002	LL	2.82	0.002	LL
Guangdong	1.86	0.036	HH	2.19	0.026	HH
Hebei	2.10	0.002	LL	2.14	0.002	LL
	Table	3 The re	sults of Ho	otspot Getis	-Ord, Gi*	
Province	China ref	erence		WHO refe	erence	
	Z Score	P Value	Gi-Bin	Z Score	P Value	Gi-Bin
Zhejiang	-1.98	0.048	-2	-1.79	0.074	-1
Yunnan	3.94	0.000	3	4.16	0.000	3
Xinjiang	0.73	0.462	0	0.39	0.698	0
Sichuan	3.19	0.001	3	3.12	0.002	3
Shaanxi	0.12	0.905	0	0.17	0.866	0
Shanxi	-2.53	0.011	-2	-2.55	0.011	-2
Shandong	-3.45	0.001	-3	-3.42	0.001	-3
Qinghai	1.23	0.219	0	0.95	0.342	0
Ningxia	-0.40	0.687	0	-0.58	0.561	0
Inner						
Mongolia	-2.04	0.042	-2	-2.09	0.037	-2
Liaoning	-2.85	0.004	-3	-2.85	0.004	-3
Jiangxi	0.91	0.364	0	1.16	0.248	0
Jilin	-2.56	0.010	-2	-2.55	0.011	-2
Hunan	2.04	0.042	2	2.28	0.022	2
Hubei	-0.05	0.957	0	0.19	0.846	0
Heilongjiang	-1.07	0.283	0	-1.11	0.267	0
Henan	-0.61	0.542	0	-0.47	0.638	0
Beijing	-3.17	0.002	-3	-3.19	0.001	-3
Tianjin	-3.17	0.002	-3	-3.19	0.001	-3
Hainan	2.94	0.003	3	3.12	0.002	3
Guizhou	3.23	0.001	3	3.38	0.001	3
Guangxi	3.21	0.001	3	3.41	0.001	3
Gansu	1.87	0.061	1	1.64	0.102	0
Fujian	0.52	0.602	0	0.78	0.435	0
Anhui	-2.23	0.026	-2	-2.06	0.039	-2
Shanghai	-3.15	0.002	-3	-3.00	0.003	-3
Chongqing	2.45	0.014	2	2.54	0.011	2
Jiangsu	-3.12	0.002	-3	-3.01	0.003	-3

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Guangdong	1.97	0.049	2	2.21	0.027	2	
Hebei	-3.17	0.002	-3	-3.19	0.001	-3	



Figure 1 The discrepancy of prevalence between different age groups in different regions. 1 represents developed region; 2 represents Intermediately developed region; 3 represents under-developed region. A is according Chinese growth reference; B is according WHO growth reference.

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Spatial and Demographic Disparities in Short Stature among Schoolchildren aged 7-18 years: a Nation-wide Survey in China, 2014

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Abstract **Objectives:** To identify spatial disparities and demographic characteristics of short stature, we analyzed the prevalence of short stature collected in a nationwide health survey. **Settings:** Data were obtained from the 2014 CNSSCH (a cross-sectional study of China). Participants came from 30 provinces, autonomous regions, and municipalities (except Tibet, Hong Kong, Macao, and Taiwan). **Participants:** There were 213,795 Han schoolchildren between 7–18 years old enrolled in our study. All participants were sampled by stratified cluster. Primary and secondary outcome measures: Short stature; Chinese and WHO age- and gender-specific height growth references were used for short stature assessment. **Results:** The age-standardized and age-gender-standardized prevalence of short stature nationwide was 3.70 and 2.69% according to Chinese and WHO growth references, respectively. The short stature prevalence differed significantly among age groups, urban and rural areas, and regions with different socioeconomic development levels (all p < p0.0001). The prevalence was 2.23% in urban versus 5.12% in rural areas (p < 0.001). The prevalence was 2.60% in developed, 3.72% in intermediately-developed, and 4.69% in under-developed regions (p < 0.0001). This was all according to China's growth reference, but similar patterns were observed on prevalence based on the WHO reference. The spatial distribution of prevalence of short stature presented a clustered pattern. Moran's I value was 0.474 (p < 0.001) and 0.478 (p < 0.001) according to the Chinese and WHO growth references, respectively. The southwest part of China showed a higher prevalence of short stature, whereas lower prevalence of short stature was observed mainly in the northeast part of China. **Conclusions:** There is an appreciably high prevalence of short stature in rural, under-developed areas of China. There are high prevalence spatial clusters of short

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3 4	1	stature in southwestern China. This provides corroborating evidence for a tailored
5 6	2	strategy on short stature prevention and reduction in special areas.
7 8	3	
9 10	4	Strengths and Limitations of This Study
11 12	5	This is the first study to detect the spatial discrepancy of prevalence of short stature
13 14	6	in mainland China.
15 16	7	The results provide corroborating evidence for a tailored strategy on short stature
17 18	8	prevention and reduction in special areas.
19 20	9	Our study raises a discussion that, because of the geographical and climatic
21 22	10	differences between north and south China, we may need to consider regional differences
23 24	11	in height when we diagnose short stature.
25 26	12	Our study is a cross-sectional study. We did not explore the cause of short stature
27 28	13	and did not perform a follow-up to learn the adult heights of our participants.
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1 Introduction

Short stature is a major morbid condition for children who are referred to pediatric endocrinologists.¹⁻³ About half of new visits to the pediatric endocrine department are harassed by short stature.⁴ It is usually caused by multiple factors, including children's nutritional status, repeated infections due to unsanitary environmental conditions, and the existence of several unknown endocrine metabolic disorders.⁵ The causes of short stature are a wide spectrum and mainly divided into normal (e.g., familial short stature and constitutional delay of growth) and pathological (e.g., growth hormone deficiency, Turner syndrome, hypothyroidism, chronic diseases, idiopathic short stature, etc.).⁶ It is regrettable that some of the causes of morbid status remained unidentified, this is what we call idiopathic short stature. With the advancement of molecular diagnostic techniques, some unexplained causes for short stature have been gradually revealed. It can somewhat be attributed to genetic variation, indicating short stature as a phenotype of genetic diseases.⁴ Additionally, short stature affects children's physical and mental health. Children with short stature tend to suffer psychological disorders, such as low self-esteem, academic difficulties, social immaturity etc.⁷ Short stature can still affect children's health after they grow up. For instance, females with short stature were susceptible to have preterm birth when they became pregnant in adulthood.⁸ Therefore, identifying short stature in childhood is extremely important for physical and mental illness reduction and should be an imperative part of children's health programs.

The prevalence of short stature varies greatly among different regions due to diverse social development and natural environment.⁹⁻¹² It has been reported that children living in undeveloped areas were more likely to have stunted growth (or short stature). In 2017, the data showed that the prevalence of stunting in children under five years old in East and South Africa and South Asia was 34.1 and 35%, respectively.¹³ Another study showed that children in north China were taller, on average, than children in south China.¹⁴ In addition, children living in economically developed areas such as Hong Kong

(located in the south of China) were also susceptible to a certain percentage of short stature, indicating that there are other reasons that cause short stature.¹⁵ For example, geographical and climate factors may play an important role in short stature. Is there a special spatial distribution of short stature in mainland China? Is this distribution associated with socioeconomic or geographical characteristics? Unfortunately, data related to the geographical distribution of short stature in China is seldom reported. To fill such a gap, we analyzed the schoolchildren's height in a nationwide health survey, aiming to identify the spatial disparities and demographic characteristics of short stature. **Methods** Date Collection and Sampling Data were collected from the 2014 Chinese National Survey on Students Constitution and Health (CNSSCH), a national health survey on schoolchildren. Eligible participants were Han Chinese individuals aged 7–18 years old. The sampling procedures of CNSSCH have been reported.¹⁶ In summary, all participants were collected by stratified cluster sampling according to the principle of CNSSCH. Selected places in each province were graded into developed, intermediately-developed, under-developed levels based on the local socioeconomic development. Subsequently, children were divided into four strata: urban boys, rural boys, urban girls and rural girls. Then, 50 people were collected in each unit (for each year of age, gender, the urban/rural, developed/intermediately-developed/under-developed groups, and province). In the end, 213,795 Han schoolchildren were enrolled in our study, and they came from 30 provinces, autonomous regions, or municipalities (except Tibet, Hong Kong, Macao, and Taiwan). The 18-year-old schoolchildren of Beijing could not be divided into three classes based on the condition of socioeconomic development, so we excluded the data of this group. This study was conducted in accordance with the guidelines laid down in the Declaration of Helsinki. We obtained informed consent from parents and schoolchildren.

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1	This study was approved by the Medical Research Ethics Committee of Peking
2	University Health Science Center (IRB00001052-13082) and the Clinical Research
3	Ethics Committee of the China–Japan Friendship Hospital(2018-94-K68).
4	Anthropometric Measurements
5	Standing height (cm) was measured by trained staff following a standardized
6	procedure, which was in accordance with the anthropometry methods in the 2006 World
7	Health Organization (WHO) Child Growth Reference. ¹⁷ Height was measured to the
8	nearest 0.1 cm with portable stadiometers. Children stood without shoes, their heels were
9	together with toes apart at a 60° angle, and their backs were against a calibrated
10	backboard.
11	Short stature is defined as a height below the 3 rd centile compared to children in the
12	same age, gender, and ethnic population. ¹⁸ In this study, we used China's and WHO's
13	age- and gender-specific height growth references for short stature assessment. ¹⁹
14	Statistical Analysis
15	The demographic disparities of short stature were presented as a number (percent).
16	Prevalence was age-standardized (or age-gender-standardized) directly to the China 2000
17	Census. Direct standardization was conducted among provinces, municipalities, and
18	autonomous regions to make comparisons of short stature across regions easier to
19	interpret. The Chi-square test was conducted to assess differences in prevalence of short
20	stature among genders, age groups, urban/rural areas, and regions of different
21	developmental levels. The Cochran-Armitage test was used for testing trend. Moran's I,
22	Getis-Ord Gi*, and Anselin Local Moran's I were performed to identify spatial
23	disparities. Getis-Ord Gi* and Anselin Local Moran's I results were displayed on maps.
24	Moran's I proposed by Patrick Alfred Pierce Moran in 1950, to measure spatial
25	autocorrelation. ^{20 21} Moran's I ranges from -1 to 1. ²² Values approach to zero means
26	lacking a spatial association (i.e., a random distribution), values approach to negative one
27	means spatial dispersion, and values approach to positive one means clustering. ²²

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I	Moran's I statistics with p-values less than 0.05 are considered statistically significant.				
2	Getis-Ord Gi* was proposed by Arthur Getis and Keith Ord in 1992. ²³ In our study,				
3	positive Gi * Z-scores indicate high short stature clustering, scores near 0 indicate no				
4	clustering existed, and negative scores suggest lower short stature clustering. Local				
5	Moran's I, proposed by Luc Anselin in 1995, estimates inter-cluster variation. ²⁴ We used				
6	the Anselin Local Moran's I to estimate the spatial clustering of high-high clustering,				
7	low-low clustering, low-high clustering and high-low clustering. ²² Statistical analyses				
8	were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC) and geographical				
9	disparities were analyzed by ArcMap software 10.2 (ESRI, Redlands, California, USA).				
10	p-values less than 0.05 (two-sided) were considered statistically significant.				
11	Patient and Public Involvement				
12	Participants were not involved in the design of this study.				
13					
14	Results				
15	Characteristics of Participating Children				
16	In total, 213,795 children, comprising 106,857 boys and 106,938 girls, were enrolled				
17	in our study. The participants were distributed evenly between sexes (i.e., the ratio of				
18	boys and girls was close to 1:1) and among the groups of different ages, urban-rural areas,				
19	and regions with different socioeconomic development levels (table 1).				
20					
21	Table 1 Characteristics of participating children in the national survey in 2014				
	X 7 • 11		N (70)		
	v ariables	Boys	Girls	Both	
		(n=106857)	(n= 106938)	(n=213795)	
	Age (years)				
	7	8944 (8.37)	8942 (8.36)	17886 (8.37)	
	8	8903 (8.33)	8929 (8.35)	17832 (8.34)	
	9	8962 (8.39)	8980 (8.40)	17942 (8.39)	

10	8972 (8.40)	8967 (8.39)	17939 (8.39)
11	8982 (8.41)	8937 (8.36)	17919 (8.38)
12	8953 (8.38)	8951 (8.37)	17904 (8.37)
13	8968 (8.39)	8982 (8.40)	17950 (8.40)
14	8964 (8.39)	8969 (8.39)	17933 (8.39)
15	8973 (8.40)	8987 (8.40)	17960 (8.40)
16	8960 (8.39)	8967 (8.39)	17927 (8.39)
17	8952 (8.38)	8980 (8.40)	17932 (8.39)
18	8324 (7.79)	8347 (7.81)	16671 (7.80)
Residence			
Urban	53502 (50.07)	53537 (50.06)	107039 (50.07)
Rural	53355 (49.93)	53401 (49.94)	106756 (49.93)
Socioeconomic development			
Developed	35567 (33.28)	35704 (33.39)	71271 (33.34)
Intermediately developed	35659 (33.37)	35620 (33.31)	71279 (33.34)
Under-developed	35631 (33.34)	35614 (33.30)	71245 (33.32)

Prevalence of Short Stature

The nationwide prevalence of short stature was 3.67 and 2.70% according to the Chinese and WHO growth references, respectively. Based on the Chines growth reference, short stature prevalence differed significantly among age groups, urban-rural areas, and regions with different socioeconomic development levels (all p < 0.0001). This was especially true for urban versus rural areas (i.e., 2.23 vs 5.12%, respectively; $p < 10^{-10}$ 0.0001) and regions of varying socioeconomic development (i.e., 2.60 in developed, 3.72% in intermediately-developed, and 4.69% in under-developed regions; p < 0.0001) (table 2 and figure 1A). Similar patterns were observed in the short stature prevalence
1	based on the WHO reference (table 2 and figure 1A). The age-standardized and
2	age-gender-standardized prevalence of short stature nationwide was 3.70 and 2.69%
3	according to the Chinese and WHO growth references, respectively. Notedly, the
4	prevalence of short stature defined by the Chinese reference was higher than that based
5	on the WHO reference.

7 Table 2 Prevalence of short stature in boys and girls according to China and

8 WHO references

S4	Prevalence, %			
Stratification	Both	Boys	Girls	
	China reference	e		
Age group (years)				
7-9	1646 (3.07)	843 (3.14)	803 (2.99)	
10-12	1878 (3.49)	867 (3.22)	1011 (3.76)	
13-15	2396 (4.45)	1387 (5.16)	1009 (3.75)	
16-18	1927 (3.67)	874 (3.33)	1053 (4.00)	
P for trends	< 0.0001	< 0.0001	< 0.0001	
Residence				
Urban	2382 (2.23)	1189 (2.22)	1193 (2.23)	
Rural	5465 (5.12)	2782 (5.21)	2683 (5.02)	
P-value for difference	< 0.0001	< 0.0001	< 0.0001	
Socioeconomic development				
Developed	1851 (2.60)	928 (2.61)	923 (2.59)	
Intermediately developed	2652 (3.72)	1341 (3.76)	1311 (3.68)	
Under-developed	3344 (4.69)	1702 (4.78)	1642 (4.61)	
P for trends	< 0.0001	< 0.0001	< 0.0001	
Total	7847 (3.67)	3971 (3.72)	3876 (3.62)	
	WHO reference	e		
Age group (years)				
7-9	776 (1.45)	331 (1.23)	445 (1.66)	
10-12	994 (1.85)	164 (0.61)	830 (3.09)	
13-15	1525 (2.83)	718 (2.67)	807 (3.00)	
16-18	2485 (4.73)	1152 (4.39)	1333 (5.07)	

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P for trends	< 0.0001	< 0.0001	< 0.0001
Residence			
Urban	1823 (1.70)	754 (1.41)	1069 (2.00)
Rural	3957 (3.71)	1611 (3.02)	2346 (4.39)
P-value for difference	< 0.0001	< 0.0001	< 0.0001
Socioeconomic development			
Developed	1377 (1.93)	549 (1.54)	828 (2.32)
Intermediately developed	1979 (2.78)	821 (2.30)	1158 (3.25)
Under-developed	2424 (3.40)	995 (2.79)	1429 (4.01)
P for trends	< 0.0001	< 0.0001	< 0.0001
Total	5780 (2.7)	2365.00 (2.21)	3415 (3.19)

We did not observe a gender difference in ov prevalence of short stature according to the Chinese growth reference (p = 0.) . However, we observed this difference in prevalence evaluated by the WHO g h reference (p < 0.0001). Because we found significant differences of prevalence of t stature in urban and rural areas and regions with different socioeconomic develop t levels, we then explored further to see if a gender difference of short stature existed ferent areas and regions. Based on the Chinese reference, results (table 3) showed that ere are no significant differences in prevalence of short stature between genders in urb or rural areas or in regions of different socioeconomic development levels. Acco ng to the WHO reference, there are significant differences in gender between urban of al areas and among all the regions of different socioeconomic development levels.

Table 3Discrepancy of genders in different r ence and regions

Stratification	China reference		WHO reference	
Stratification	χ^2	p value	χ^2	p value
Residence				
Urban	0.004	0.947	55.163	< 0.0001
Rural	1.981	0.159	141.122	< 0.0001

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Intermediately developed	0.319	0.572	59.406	< 0.0001
Under-developed	1.100	0.294	80.656	< 0.0001
Total	1.270	0.260	195.227	<0.0001

Then, we drew trajectories of prevalence of short stature across different ages for boys and girls in different areas of residence (urban/rural) and regions (i.e., developed, intermediately-developed, or under-developed) (figure 1B and C, and Supplementary figure 1). The high prevalence of short stature in rural or undeveloped regions are consistent across all ages. In addition, we had two interesting findings that applied to all children no matter whether they lived in urban or rural areas or regions of different socioeconomic development levels. The first is that, in most cases, although the trajectories of short stature prevalence in different age groups fluctuated, and the lowest point was always in the 10–12 age group for boys and in the 7–9 age group for girls. The second finding is that, in most cases, the peak of prevalence of short stature appeared after the lowest point. Some of them followed closely in the next age group while others appeared in the 16–18 age group.

15 Spatial Characteristics of Short Stature

The spatial distribution of prevalence of short stature presented a clustered pattern. Moran's I value was 0.474 (p < 0.001) and 0.478 (p < 0.001) according to the Chinese and WHO growth references, respectively. The maps of prevalence of short stature (figures 2A, 2B and Supplementary table 1) indicated that the distribution of prevalence was spatially different. Southwest China showed higher prevalence of short stature while northeast China had comparatively lower prevalence. Anselin Local Moran I indicated that there was a high-high cluster in Sichuan, Guizhou, Guangxi, Guangdong, Chongqing, Hainan, Hunan, and Yunnan. A low-low cluster existed in some other provinces like Liaoning, Jilin, Inner Mongolia, Beijing, Tianjin, Hebei, Shanxi, Shandong, Jiangsu,

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Shanghai, Zhejiang, and Anhui (figures 2C, 2D and Supplementary table 2). These results were consistent between the two references. According to the Chinese growth reference, Getis-Ord Gi* identified the following as hotspot-99% confidence areas: Sichuan, Yunnan, Guizhou, Guangxi, and Hainan. The hotspot-95% confidence areas were Chongqing, Hunan, and Guangdong. The hotspot-90% confidence area was Gansu. The coldspot-99% confidence areas were Liaoning, Beijing, Tianjin, Hebei, Shandong, Shanghai, and Jiangsu. The coldspot-95% confidence areas were Zhejiang, Anhui, Jilin, Inner Mongolia, and Shanxi (figure 2E and Supplementary table 3). According to the WHO growth reference, Getis-Ord Gi* identified the following hotspot-99% confidence areas: Sichuan, Yunnan, Guizhou, Guangxi, and Hainan. The hotspot-95% confidence areas were Chongging, Hunan, and Guangdong. The coldspot-99% confidence areas were Liaoning, Beijing, Tianjin, Hebei, Shandong, Shanghai, and Jiangsu. The coldspot-95% confidence areas were Anhui, Jilin, Inner Mongolia, and Shanxi. The coldspot-90% confidence area was Zhejiang (figure 2F Supplementary table 3).

Discussion

In our study, the age-standardized and age-gender-standardized prevalence of short stature nationwide was 3.70 and 2.69% according to Chinese and WHO growth references, respectively. Regarding the terminology of short stature, it is sometimes synonymous to "stunted growth" and also known as stunting or nutritional stunting in children. According to WHO, stunting is defined as a Height-for-age Z-score (HAZ) <-2SD (Standard Deviations) of the WHO Child Growth References.²⁵ In China, the definition of short stature is a height-for-age below the third centile (-1.88 SD) or less than 2 SD compared to average height of children of the same age and gender.¹⁸ Globally, the prevalence of stunting under five years old declined from 32.6 to 22.2% between 2000 to 2017.¹³ One study in 2014 showed that the crude prevalence of stunting in Chinese schoolchildren between 7-18 years old was 2.3% based on the WHO growth

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1	reference, which is lower than our result. This difference could be partly attributed to the
2	different SD adopted in our study. We used the third centile (-1.88 SD) to define short
3	stature, which is currently routine clinical practice in China. In Song's study, -2 SD was
4	used to assess stunting, which may have contributed to less diagnoses and a lower
5	prevalence compared to our study. Their study also showed that, from 1985 to 2014, the
6	national crude prevalence of stunting in Chinese schoolchildren decreased from 16.4 to
7	2.3%. ²⁶ Another study in Hong Kong processed in 2005 showed that the crude prevalence
8	of short stature (i.e., height below the third centile) was 1.7% in 6-10 year-old children
9	and was 4.4% in 11–18 year-olds based on the WHO growth reference. World Bank data
10	showed that the prevalence of stunting in 2015 among children under 5 years old in South
11	Asia, Sub-Saharan Africa, the Middle East and North Africa, East Asia and the Pacific,
12	Latin America and the Caribbean, and Europe and Central Asia was 36.2, 35.2, 15.8, 14.4,
13	10.1, and 9.2%, respectively. ²⁷ In conclusion, the total prevalence of short stature among
14	Chinese schoolchildren being low and having a decreased trend may reflect
15	improvements in many aspects of China in recent years. The prevalence of short stature
16	helps us to know the nutritional and pathological condition of children and provide useful
17	data to decision makers .
18	The prevalence of short stature was considerably higher in rural areas than in urban
19	ones. The prevalence in the former was nearly 2.5 times higher than in the latter. With
20	respect to regions with different socioeconomic development levels, we observed a
21	climbing trend of short stature in under- and intermediately-developed regions compared
22	to developed ones. Both the higher prevalence in rural areas and less developed regions
23	indicated that children living in socioeconomically delayed areas were at a higher risk of
24	having stunted growth. Based on the WHO growth reference, the prevalence of stunting
25	in children was 16.4% and 5.7% in rural and urban China respectively in 2002.28
26	Economic development of China does not reduce inequalities in nutrition and health care
27	services. ²⁹ A study has shown that there have been declining trends of urban–rural

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disparities since China's Reform and Opening Policy was established in 1978.³⁰ However, the difference in the prevalence of short stature in rural and urban areas is still a concern. This inequality reminds us of the need for policies to be implemented in this area. Our study has shown differences in prevalence between age groups. These differences may be mainly because the increase of height in human beings does not occur at a constant velocity. The highest growth rate occurs in fetal life and infancy, then slows down during childhood, and the acceleration happens during puberty.³¹ The acceleration of the rate of height growth in puberty can partly explain the differences in prevalence of short stature between in different age groups. When does puberty begin in Chinese adolescents? Girls may begin puberty earlier than boys.^{32 33} One study showed that the median age of menarche in Chinese girls was 12.47 years in 2010.³⁴ Puberty starts almost two years before the age of menarche in girls. The median age of puberty onset (i.e., testicular volume is 4 mL or greater) in urban Chinese boys was 10.55 years between 2003 and 2005.³⁵ Another study showed the menarche of Hong Kong Chinese girls occurred at 12.1 years, and the first nocturnal ejaculation occurred at 13.0 years for Hong Kong Chinese boys in 1996.³⁶ The timing of puberty reported by literature is consistent with our study results. The lowest point of prevalence of short stature occurred in the 10-12 age groups for boys and 7-9 age groups for girls, respectively. During these ages, Chinese boys and girls start puberty. The rate of height growth accelerated, and the prevalence of short stature lowered correspondingly. The phenomena of the peak appearing after the lowest point may indicate that, after puberty, the growth rate gradually decreased in these age groups, especially in the 16–18 age group. One study showed that most Chinese children will stop height growth by the time they reach 18 years of age.¹⁹ On account of these changes in the height growth rate during puberty, the diagnosis of short stature may be prudent for children between 7 to 18 years old. As for gender differences in prevalence of short stature, the two growth references gave opposite results. We found that, in the 10-12 age group, the prevalence of short

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stature in boys based on the WHO reference was low at 0.61% (figure 2). We think that the reason behind this is related to the acceleration of puberty in Chinese boys of this age group and to the fact that the data of the WHO reference did not detect boys who are really short stature. Two studies in Argentinian and Polish children showed growth variations, especially in adolescents, when comparing the WHO growth reference data with the recommend national references for clinical use.^{37 38} Another study showed that Asian subpopulations have an earlier onset of puberty than other ethnic groups.³⁹ In conclusion, using US children pubertal growth patterns (i.e., WHO reference for 5-19 years based on the data of the US population) to assess Chinese children pubertal growth patterns may be inappropriate. We recommend the use of the Chinese growth reference for clinical assessment of Chinese adolescent. In terms of spatial distribution, our study showed that the prevalence of short stature was higher in southwest of China but lower in northeast China. With the development of the geographic information system (GIS) technique, the research on the spatial distribution for diseases has gradually attracted people's attention.^{22 40-43} A study from Somalia shows that there is a high prevalence of stunting in the south area of the country, especially around the two main rivers of Juba and Shebelle.¹¹ There is a study in Ethiopia showing that they identified clusters of high prevalence of stunting in the eastern part and clusters of low prevalence in the western part of the district.¹² In our study, we tried to explore the spatial discrepancy of prevalence of short stature in mainland China using Moran's I, Getis-Ord Gi*, and Anselin Local Moran's I, which are widely used in exploring the space-time pattern of diseases. Our research shows that there is a significant difference in the prevalence of short stature in different areas of China. Specifically, there is a higher prevalence cluster for short stature in the southwestern region, especially in the Sichuan, Guizhou, Guangxi, Guangdong, Chongqing, Hainan, and Yunnan provinces. In the northeast region, there was a lower prevalence cluster for short stature, especially in Inner Mongolia, Beijing, Tianjin, Hebei, Liaoning, Jilin, Shandong, Shanxi, Shanghai,

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Zhejiang, Anhui, and Jiangsu. What accounts for this spatial discrepancy?
Socio-economic factors may account for something.^{44 45} Two studies about spatial
difference of stunting mentioned above found that maternal education and food security
and access were associated with stunting.^{11 12} In addition, the discrepancies in some
disease conditions, such as repeated infections and endocrine metabolic disease, may
affect the distribution of short stature. It is a complicated situation, and we hope we can
deeply research this in future studies.

Another study that caught our attention found that, in mainland China, children of 7 to 18 years old living in the north had a higher height than children in the south on average.¹⁴ The maximum height difference of different regions was almost 4 to 5 cm.¹⁴ China is not a country of immigrants. Residents have lived here for thousands of years, and residents and the natural environment have developed adaptations. Because there is a disparity in the geographic and climatic environment between south and north China, we believe that the geographic and climatic factor may play an important role in short stature. Firstly, altitudes may be an important factor for height growth and is associated with short stature. Peruvians and Tibetans lived at high altitude places and tend to be short.⁴⁶⁻⁴⁸ Because of the high altitude environment, the body's functions will exhibit high-altitude adaptations, such as larger lungs, better lung function, lower blood hemoglobin concentration, etc., that may not be found in lowlanders.⁴⁹ Short stature may be another type of adaption because animals living in high elevations tend to be smaller to adapt to an environment with a scarcity of food.⁴⁶ Even European settlers living in the Andes had statures 1–5 cm shorter than their compatriots living in lowland areas.⁵⁰ Moreover, temperature, rainfall, and extreme weather events (floods/droughts) were reported to be associated with short stature.⁵¹⁻⁵³ Regrettably, we did not explore the causes of short stature. The geographic and climatic factor may determine short stature to some degree. Therefore, children who live in hotspot areas (some places in southwestern China) will be diagnosed with short stature though they do not have a pathological condition. The

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prevalence of short stature will be overestimated. The solutions for this are to build
growth reference based on the same area population or lower the cut-off value to
diagnose short stature in these places⁴⁸. We must be more prudent when we diagnose
short stature of children from these areas and avoid excessive laboratory tests or therapy
for these children. Further studies on this subject are needed, and we hope our study is
raising a discussion on the topic.

7 Limitations

Height varies between different population groups worldwide.^{54 55} The Dutch population is the tallest and the Peruvian population is the shortest population in the word.^{46 56} Even immigrants will retain genetic potential for height, as observed in Turkish children.⁵⁷ The definition of short stature emphasizes that the comparison of height needs to be between the same population group, race, or ethnicity.⁵⁸ There are 56 ethics groups (nationalities) in China, as shown by the 2011 National Population Census data. Of the Chinese population, 91.51% are of Han nationality and 8.49% are of "minority nationalities".⁵⁹ A study compared the height of minority nationalities with Han schoolchildren in southwest China. Results showed that the age of the rapid growth period in the southwest China minority nationality group was greater than that in the Han schoolchildren.⁶⁰ Another study showed that the stunting prevalence of Tibetan children in Lasa (Tibet) was higher than the national prevalence.⁶¹ Based on the above, the adult height or growth pattern of some minority nationalities may differ from the Han nationality in China, and it may be insightful to know the condition of short stature in these ethnic minorities to see if it is any different to other groups (i.e., the Han nationality or other nationalities) who live in same geographical environment. Although we did not evaluate the short stature of ethnic minorities in our study, it is a meaningful research direction for later scholars. In our study, we also did not exclude the effect of the floating population (i.e., individuals whose growth place and birth place are not the same).

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Because our study is cross-sectional, we also did not explore the causes of short stature and we did not perform a follow-up to learn the adult heights of our participants.

Conclusions

There is an appreciably high prevalence of short stature in rural, under-developed areas of China. This provides corroborating evidence for a tailored strategy for short stature prevention and reduction in special areas. We also uncover that there are high prevalence spatial clusters of short stature in the southwestern China, such as Sichuan, Guizhou, Guangxi, Guangdong, Chongqing, Hainan, Yunnan provinces. Therefore, further study needs to be done in these places to detect the cause of short stature. Our results indicate that, aside from the racial factor, the regional factor may need to be considered when defining short stature.

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20 Contributors

21 Zhixin Zhang and Jun Ma worked together to develop the research question, study
22 design and analytic plan. Yanhui Dong and Zhaogeng Yang collected and collated data of
23 prevalence of short stature in different genders, regions, ages groups from CNSSCH data.
24 Jia Ma wrote the manuscript. Fen Dong analyzed demographic characteristics of data by
25 mathematical statistics and revised the manuscript. Tao Pei, Jie Chen, Sihui Guo analyzed
26 spatial distribution of prevalence of short stature and Tao Pei helped to revised the

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2	check the data. All authors have contributed to the work and approved the manuscript.
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9	
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10	Etines approval. Informed consent was obtained from both parents and schoolenhare
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12	Ethics Committee of Peking University Health Science Center (IRB00001052-13082)
13	Clinical Research Ethics Committee of China-Japan Friendship Hospital (2018-94-K6
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15	Data sharing statement: No additional data are available.
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3	1	Figure Legends
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8	4	A. The discrepancy of prevalence between urban-rural and different regions.
9	5	B. The discrepancy of prevalence between different age groups according China growth reference.
10	6	C. The discrepancy of prevalence between different age groups according WHO growth reference.
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12	8	Figure 2
13 14	9	A. The distribution of standardized prevalence according China growth reference.
15	10	B The distribution of standardized prevalence according WHO growth reference
16	11	C. The results of Appelin Local Moran's Labout standardized prevalence according China growth
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19 20	13	D. The results of Anselin Local Moran's I about standardized prevalence according wHO growth
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22	15	E. The result of Hotspot Getis-Ord, Gi* about standardized prevalence according China growth
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A.The discrepancy of prevalence between urban-rural and different regions. B.The discrepancy of prevalence between different age groups according China growth reference. C.The discrepancy of prevalence between different age groups according WHO growth reference. BMJ Open: first published as 10.1136/bmjopen-2018-026634 on 16 July 2019. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.



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Supplementary

		provinces				
Province	China	a reference	WHO	WHO reference		
	N (%)	Age-standardized prevalence, %	N (%)	Age-gender standardized prevalence, %		
Beijing	41 (0.62)	0.64	22 (0.33)	0.31		
Tianjin	54 (0.75)	0.77	38 (0.53)	0.52		
Hebei	93 (1.29)	1.30	77 (1.07)	1.05		
Shanxi	222 (3.08)	3.14	152 (2.11)	2.12		
Inner Mongolia	134 (1.90)	1.91	94 (1.33)	1.31		
Liaoning	79 (1.10)	1.10	60 (0.83)	0.83		
Jilin	129 (1.81)	1.82	91 (1.28)	1.29		
Heilongjiang	205 (2.86)	2.80	134 (1.87)	1.81		
Shanghai	60 (0.84)	0.82	43 (0.60)	0.60		
Jiangsu	50 (0.72)	0.74	38 (0.55)	0.57		
Zhejiang	93 (1.30)	1.30	83 (1.16)	1.14		
Anhui	151 (2.10)	2.10	121 (1.68)	1.67		
Fujian	81 (1.13)	1.14	57 (0.79)	0.79		
Jiangxi	287 (4.00)	4.06	214 (2.98)	2.97		
Shandong	30 (0.42)	0.42	31 (0.43)	0.43		
Henan	127 (1.76)	1.79	93 (1.29)	1.28		
Hubei	178 (2.53)	2.59	120 (1.70)	1.75		
Hunan	345 (4.80)	4.82	281 (3.91)	3.83		
Guangdong	355 (4.93)	4.95	276 (3.83)	3.78		
Guangxi	472 (6.84)	6.86	380 (5.51) 🛀	5.43		
Hainan	539 (7.49)	7.40	403 (5.60)	5.45		
Chongqing	522 (7.25)	7.37	407 (5.65)	5.61		
Sichuan	620 (8.61)	8.66	477 (6.63)	6.52		
Guizhou	972 (13.51)	13.61	725 (10.07)	10.04		
Yunnan	337 (4.68)	4.64	247 (3.43)	3.38		
Shaanxi	454 (6.32)	6.46	320 (4.46)	4.45		
Gansu	244 (3.39)	3.49	167 (2.32)	2.34		
Qinghai	446 (6.20)	6.31	275 (3.82)	3.83		
Ningxia	235 (3.42)	3.45	158 (2.30)	2.30		
Xinjiang	292 (4.11)	4.09	196 (2.76)	2.69		

Table	1 The prevalence and standardize prevalence of short stature in
	provinces

Province	Cl	nina referer	ice	WHO reference			
	Z Score	P Value	Туре	Z Score	P Value	Туре	
Zhejiang	1.99	0.008	LL	1.82	0.024	LL	
Yunnan	4.23	0.002	HH	4.31	0.002	HH	
			Not			Not	
Xinjiang	0.87	0.258	Significant	0.60	0.214	Significant	
Sichuan	3.48	0.002	HH	3.71	0.002	HH	
			Not			Not	
Shaanxi	-0.08	0.492	Significant	-0.09	0.47	Significant	
Shanxi	2.37	0.008	LL	2.38	0.004	LL	
Shandong	3.52	0.002	LL	3.36	0.002	LL	
			Not			Not	
Qinghai	0.74	0.214	Significant	0.64	0.24	Significant	
			Not			Not	
Ningxia	-0.20	0.396	Significant	0.01	0.458	Significant	
Inner							
Mongolia	2.17	0.008	LL	2.18	0.004	LL	
Liaoning	2.75	0.002	LL	2.67	0.002	LL	
			Not			Not	
Jiangxi	-0.11	0.466	Significant	0.09	0.444	Significant	
Jilin	2.03	0.006	LL	1.97	0.006	LL	
Hunan	2.05	0.02	HH	2.47	0.014	HH	
			Not			Not	
Hubei	-0.39	0.348	Significant	-0.62	0.288	Significant	
			Not			Not	
Heilongjiang	0.98	0.198	Significant	0.99	0.15	Significant	
			Not			Not	
Henan	1.12	0.138	Significant	1.07	0.15	Significant	
Beijing	2.04	0.002	LL	1.90	0.002	LL	
Tianjin	2.27	0.002	LL	2.32	0.002	LL	
Hainan	2.69	0.014	HH	3.02	0.01	HH	
Guizhou	3.65	0.002	HH	3.91	0.002	HH	
Guangxi	3.62	0.002	HH	4.12	0.002	HH	
			Not			Not	
Gansu	-1.65	0.066	Significant	-1.54	0.088	Significant	
			Not			Not	
Fujian	0.08	0.494	Significant	-0.18	0.406	Significant	

Table2The results of Anselin Local Moran's I

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Anhui	2.43	0.002	LL	2.39	0.008	LL	
Shanghai	2.52	0.002	LL	2.39	0.002	LL	
Chongqing	3.23	0.002	HH	3.45	0.002	HH	
Jiangsu	2.97	0.002	LL	2.82	0.002	LL	
Guangdong	1.86	0.036	HH	2.19	0.026	HH	
Hebei	2.10	0.002	LL	2.14	0.002	LL	

Abbreviations: HH: High-High cluster; LL: Low-Low cluster.

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	Table 5	1 ne res		spot Octis	-010, 01		
Province	C	hina reference			WHO reference		
	Z Score	P Value	Gi-Bin	Z Score	P Value	Gi-Bin	
Zhejiang	-1.98	0.048	-2	-1.79	0.074	-1	
Yunnan	3.94	0.000	3	4.16	0.000	3	
Xinjiang	0.73	0.462	0	0.39	0.698	0	
Sichuan	3.19	0.001	3	3.12	0.002	3	
Shaanxi	0.12	0.905	0	0.17	0.866	0	
Shanxi	-2.53	0.011	-2	-2.55	0.011	-2	
Shandong	-3.45	0.001	-3	-3.42	0.001	-3	
Qinghai	1.23	0.219	0	0.95	0.342	0	
Ningxia	-0.40	0.687	0	-0.58	0.561	0	
Inner Mongolia	-2.04	0.042	-2	-2.09	0.037	-2	
Liaoning	-2.85	0.004	-3	-2.85	0.004	-3	
Jiangxi	0.91	0.364	0	1.16	0.248	0	
Jilin	-2.56	0.010	-2	-2.55	0.011	-2	
Hunan	2.04	0.042	2	2.28	0.022	2	
Hubei	-0.05	0.957	0	0.19	0.846	0	
Heilongjiang	-1.07	0.283	0	-1.11	0.267	0	
Henan	-0.61	0.542	0	-0.47	0.638	0	
Beijing	-3.17	0.002	-3	-3.19	0.001	-3	
Tianjin	-3.17	0.002	-3	-3.19	0.001	-3	
Hainan	2.94	0.003	3	3.12	0.002	3	
Guizhou	3.23	0.001	3	3.38	0.001	3	
Guangxi	3.21	0.001	3	3.41	0.001	3	
Gansu	1.87	0.061	1	1.64	0.102	0	
Fujian	0.52	0.602	0	0.78	0.435	0	
Anhui	-2.23	0.026	-2	-2.06	0.039	-2	
Shanghai	-3.15	0.002	-3	-3.00	0.003	-3	
Chongqing	2.45	0.014	2	2.54	0.011	2	
Jiangsu	-3.12	0.002	-3	-3.01	0.003	-3	
Guangdong	1.97	0.049	2	2.21	0.027	2	
Hebei	-3.17	0.002	-3	-3.19	0.001	-3	

Table 3 The results of Hotspot Getis-Ord, G	The results of Hotspot Getis-Or	d, Gi*
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1 represents developed region; 2 represents Intermediately developed region; 3 represents under-developed region. A is according Chinese growth reference; B is according WHO growth reference.



STROBE Statemer	it—cn	ecklist of items that should be included in reports of observational studies	026634 or including		
	Item No.	Recommendation	for uses	Relevant text from manuscript	
Fitle and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	2019. refate	Line 5	
		(b) Provide in the abstract an informative and balanced summary of what was done and what was	Dowr Dowr d fô t	Line2-4	
		found	nloaded Superie Superie	Line26-27	
ntroduction		$\mathcal{D}_{\mathcal{D}_{\mathcal{D}_{\mathcal{D}_{\mathcal{D}}}}}$	from data		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	http:// 3ES) .	Line1-27	
Dbjectives	3	State specific objectives, including any prespecified hypotheses	j, AAntr	Line5-7	
Methods		VIQ.	en.bmj aining,		
Study design	4	Present key elements of study design early in the paper	affd s	Line14-15	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	on June	Line16-27	
Participants	6	(<i>a</i>) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	13, 2025 <i>a</i>	Line16-23	
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	it Agence s.		
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	Bibliogra		

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		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed	n-2018-0266	
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	34 on 16 Ju Ei	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers.	ly 2019. C	Line14-16
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	o o ent Super	Line8-13
Bias	9	Describe any efforts to address potential sources of bias	ieur ()	Line26-27
Study size	10	Explain how the study size was arrived at	n http ABES)	Line21-24
		I training, and similar technologies.	jopen.bmj.com/ on June 13, 2025 at Agence Bibliograph	
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Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	118-026634 1ht, includi		
Statistical	12	(a) Describe all statistical methods, including those used to control for confounding	on 16 ng for	Line18-27	
methods		(b) Describe any methods used to examine subgroups and interactions	July 2 Ense uses r	Line22	
		(c) Explain how missing data were addressed	2019. [pignem related		
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	Downlo nent S I to te	Line20-22	
		Case-control study—If applicable, explain how matching of cases and controls was addressed	oaded uperie xt and		
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	∣ from http eur (ABES ∣ data min		
		(<u>e</u>) Describe any sensitivity analyses	ing, A		
Results			open.t		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	o <mark>mj.com/</mark> o ng ^c and si	Line19	
		(b) Give reasons for non-participation at each stage	on Jun milar t		
		(c) Consider use of a flow diagram	e 13, 2 echno		
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	2025 at A _t loĝies.	Line19-22	
		(b) Indicate number of participants with missing data for each variable of interest	gence		
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	Biblio		
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	graphi		
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Case-control study—Report numbers in each exposure category, or summary measures of exposurenCross-sectional study—Report numbers of outcome events or summary measuresn(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were includedn(b) Report category boundaries when continuous variables were categorizedn	Line4-5 Line5-7
Case-control study—Report numbers in each exposure category, or summary measures of exposure Image: Case-control study—Report numbers of outcome events or summary measures Cross-sectional study—Report numbers of outcome events or summary measures Image: Cross-sectional study—Report numbers of outcome events or summary measures (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision Image: Cross-sectional study—Report numbers of outcome events or summary measures (b) Report category boundaries when continuous variables were categorized Image: Cross-sectional study = Cross-section	Line4-5 Line5-7
Cross-sectional study—Report numbers of outcome events or summary measures 0 (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision 10 (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were 10 (b) Report category boundaries when continuous variables were categorized 10	Line4-5 Line5-7
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(b) Report category boundaries when continuous variables were categorized	
	Line11
(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	ight, The	29 80 Line15-20
Discussion			uding	6
Key results	18	Summarise key results with reference to study objectives	for us п	Line23-25
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	nseignem es related	NV 2019. D
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	ent Super to text ar	Line14-27
Generalisability	21	Discuss the generalisability (external validity) of the study results	rietur (<i>i</i> nd data	to Line9-17
Other informati	on	994	ABES) a minii	ח http://
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	ng,20 Al trai	Line8-10
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Note: An Explan checklist is best u http://www.annal	ation ised i s.org	and Elaboration article discusses each checklist item and gives methodological background and published in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmed //, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at w	exampl icine.or www.stro	 Annals of Internal Medicine at Annals of Internal Medicine at Be-statement.org. Bibliographic
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