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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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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: 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.

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 stature[1]. 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 difficulties[3]. 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[4]. Therefore, identifying short stature in childhood is 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 environment[5-8]. 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 were34.1%,35%,respectively[9]. In addition, children living in economically developed areas but with low latitude were also susceptible to short stature[10], 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 average[11]. 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 published[12]. In a word，all participants were selected by stratified cluster sampling according to the principle of CNSSCH. Selected places in each 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^{o} 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 population[13]. In this study, China's age- and gender-specific height growth charts were used for short stature assessment[14].

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).

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

Variables	N (%)		
	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)

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 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 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 10~12,13~15,16~18.In 10~12 and 16~18 year groups,the prevalence of girls is higher than boys, however in 13~15 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

Stratification	Prevalence, %		
	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 median[15]. In China, definition of short stature is the height or length below the 3rd centile (-1.88 SDS) or <–2 SDS compared to children of the same age, gender, population[13].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 2017 [9]. 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 standard[11]. 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 ago[11]. 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 studies[11], -2 SDS was used to assess stunting, which would result in less diagnoses and lower prevalence compared to ours.

The discrepancy between urban-rural and different economic developmental places

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 China[16].China has made tremendous economic achievements, but this economic development does not necessarily reduce inequalities of nutrition, and health care services[17].Researchers shows that there is a declining trends of urban–rural disparities since China's Reform and Opening Policy in 1978[18],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 10~12 and 16~18 age groups, however in 13~15 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 Shebelle[7].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 western[8].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,Chongqing,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 average[11],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 prevalence of short stature will be overstate.All of we known that Peruvians are among the world's shortest people[22],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 needed.

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.

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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 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.

References

1.Murray P G, Clayton P E, Chernausek S D. A genetic approach to evaluation of short stature of undetermined cause[J]. Lancet Diabetes Endocrinol, 2018.

2.Allen D B, Cuttler L. Clinical practice. Short stature in childhood--challenges and choices[J]. N Engl J Med, 2013, 368(13):1220-1228.

3.Kim B, Mi J P. The Influence of Weight and Height Status on Psychological Problems of Elementary Schoolchildren through Child Behavior Checklist Analysis[J]. Yonsei Medical Journal, 2009, 50(3):340.

4.Derraik J G, Lundgren M, Cutfield W S, et al. Maternal Height and Preterm Birth: A Study on 192,432 Swedish Women[J]. Plos One, 2016, 11(4):e0154304.

5.Black R E, Victora C G, Walker S P, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries[J]. Lancet, 2013, 382(9890):427-451.

6.Marshall WA. Geographical and ethnic variations in human growth. Br Med Bull. 1981,37(3):273-279.

7.Kinyoki D K, Ngianga-Bakwin K, Manda S O, et al. Assessing comorbidity and correlates of wasting and stunting among children in Somalia using cross-sectional household surveys: 2007 to 2010:[J]. Bmj Open, 2016, 6(3):e009854.

8.Hagos S, Hailemariam D, Woldehanna T, et al. Spatial heterogeneity and risk factors for stunting among children under age five in Ethiopia: A Bayesian geo-statistical model.[J]. Plos One, 2017, 12(2):e0170785.

9.United Nations International Children's Emergency Fund . Malnutrition rates remain alarming: stunting is declining too slowly while wasting still impacts the lives of far too many young children https://data.unicef.org/topic/nutrition/malnutrition/. html (accessed May 2018).

10.So H K, Nelson E A, Sung R Y, et al. Implications of using World Health Organization growth reference (2007) for identifying growth problems in Hong Kong children aged 6 to 18 years[J]. Hong Kong medical journal = Xianggang yi xue za zhi / Hong Kong Academy of Medicine, 2011, 17(3):174.

11.Cai CH, Dong B, Ma J. [District differences and regional division of heights among Chinese Han children and adolescents]. Zhonghua Liu Xing Bing Xue Za Zhi. 2012;33(2):197-200

12.Research group of the physical fitness and health surveillance of Chinese school students(2016).Report on the Physical Fitness and Health Surveillance of Chinese School Students.High Education Press, Beijing, China.

13.Chinese Society of Pediatric Endocrinology and Metabolism.Guideline for diagnosis and treatment of short stature children.Chinese Journal of Pediatrics,2008, 46(6):20-21.

14.Li H, Ji C Y, Zong X N, et al. [Height and weight standardized growth charts for Chinese children and adolescents aged 0 to 18 years][J]. Zhonghua Er Ke Za Zhi, 2009, 47(7):487-492.

15.WHO.Child malnutrition.http://www.who.int/gho/health_equity/outcomes/health_equity_child_malnutrition_a.pdf

16.Li Y P, Hu X Q, Yang X G, et al. Application of the WHO growth reference (2007) to assess the nutritional status of children in China.[J]. Biomedical & Environmental Sciences, 2009, 22(2):130-135.

17.Hsiao W C, Liu Y. Economic reform and health--lessons from China[J]. New England Journal of Medicine, 1996, 335(6):430.

18.Liu H, Fang H, Zhao Z. Urban-rural disparities of child health and nutritional status in China from 1989 to 2006.[J]. Economics & Human Biology, 2013, 11(3):294-309.

19.Song Y, Ma J, Wang H J, et al. Trends of Age at Menarche and Association with Body Mass Index in Chinese School-Aged Girls, 1985-2010.[J]. Journal of Pediatrics, 2014, 165(6):1172-1177.e1.

20.Ma H M, Chen S K, Chen R M, et al. Pubertal development timing in urban Chinese boys.[J]. International Journal of Andrology, 2011, 34(5pt2):e435-e445.

21.Tanner J M, Whitehouse R H, Marubini E, et al. The adolescent growth spurt of boys and girls of the Harpenden Growth Study[J]. Annals of Human Biology, 1976, 3(2):109-126.

22.Pennisi E. High altitude may have driven short stature in Peruvians[J]. Science, 2018, 360(6390):696.

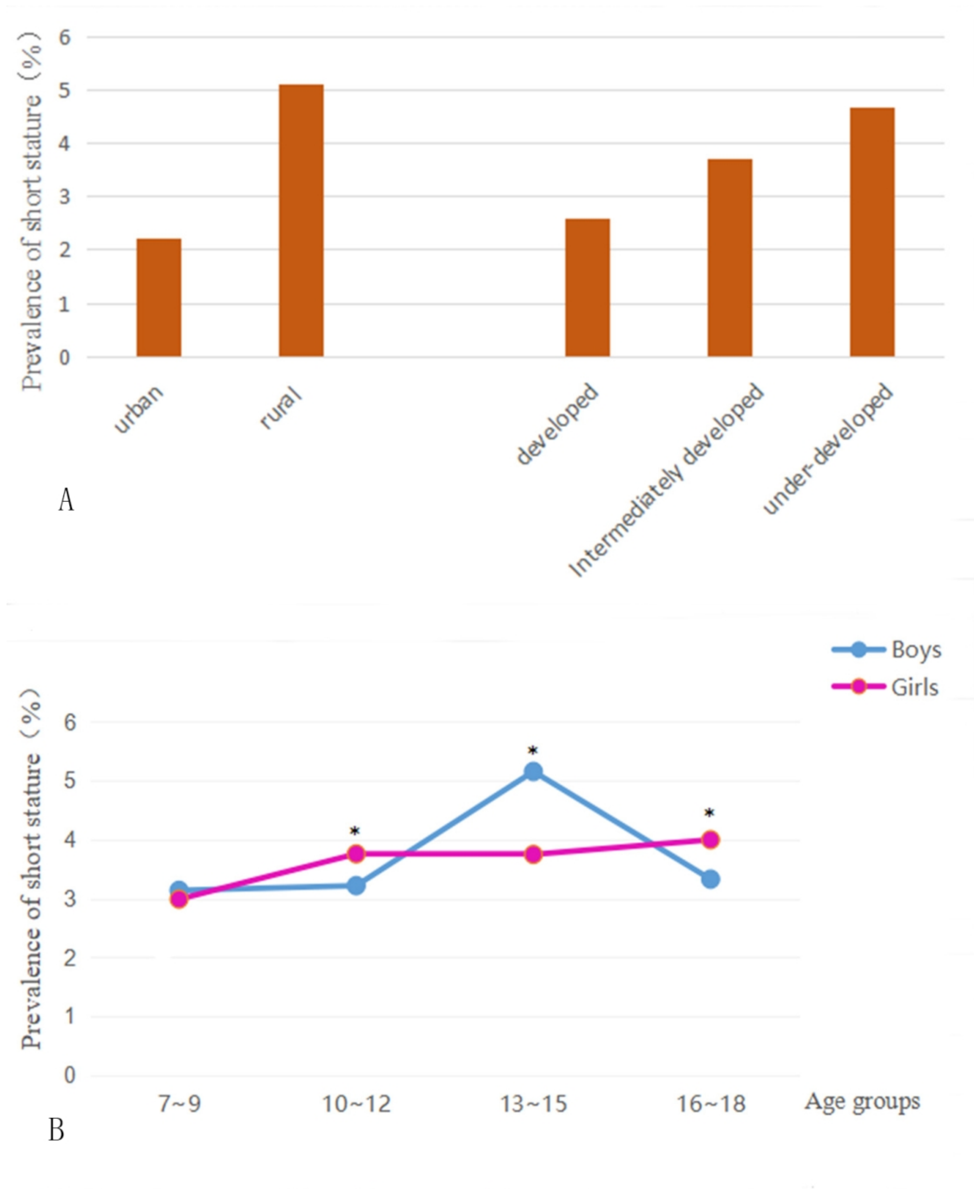

Fig.1 A.The discrepancy of prevalence between urban-rural and different economic developmental places.B.The discrepancy of prevalence between different age groups in boys and girls.In 10~12,13~15,16~18 year groups the difference are statistically significant(P=0.001,P<0.0001,P<0.0001 respectively, they were analyzed by chi-square test).

127x153mm (300 x 300 DPI)

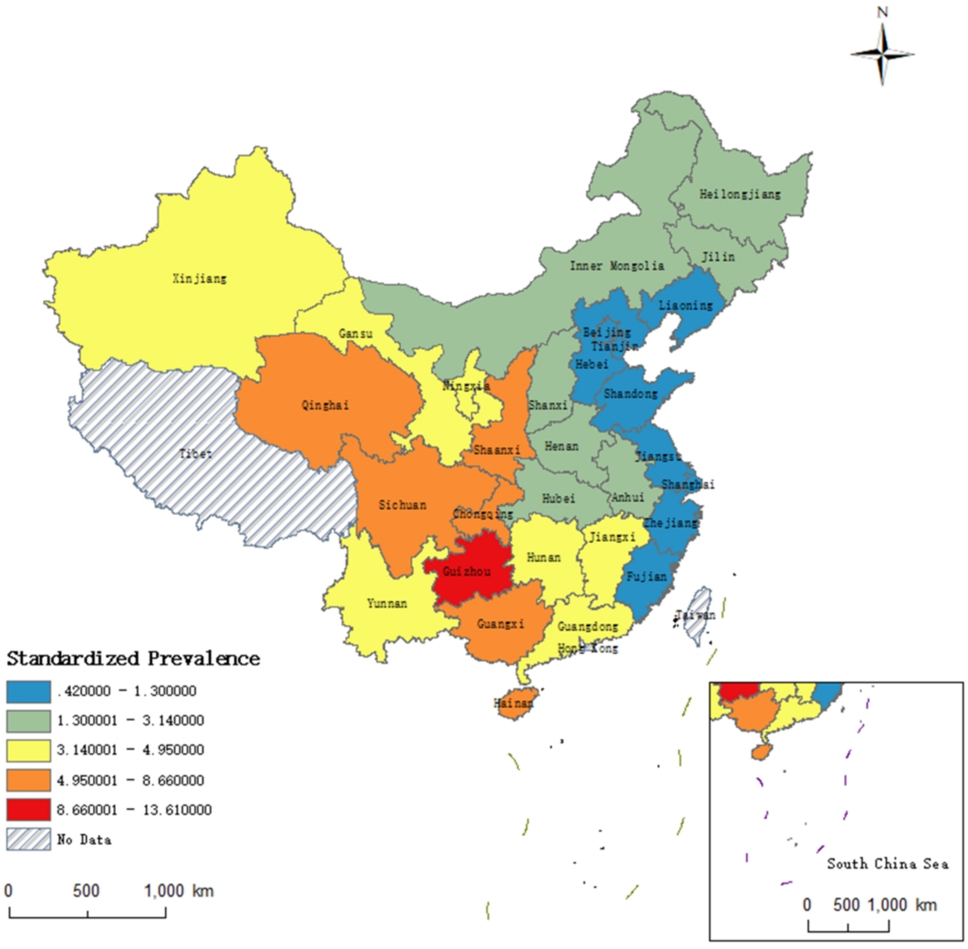

Fig.2 The distribution of short stature standardized prevalence in China (2014)

206x207mm (300 x 300 DPI)

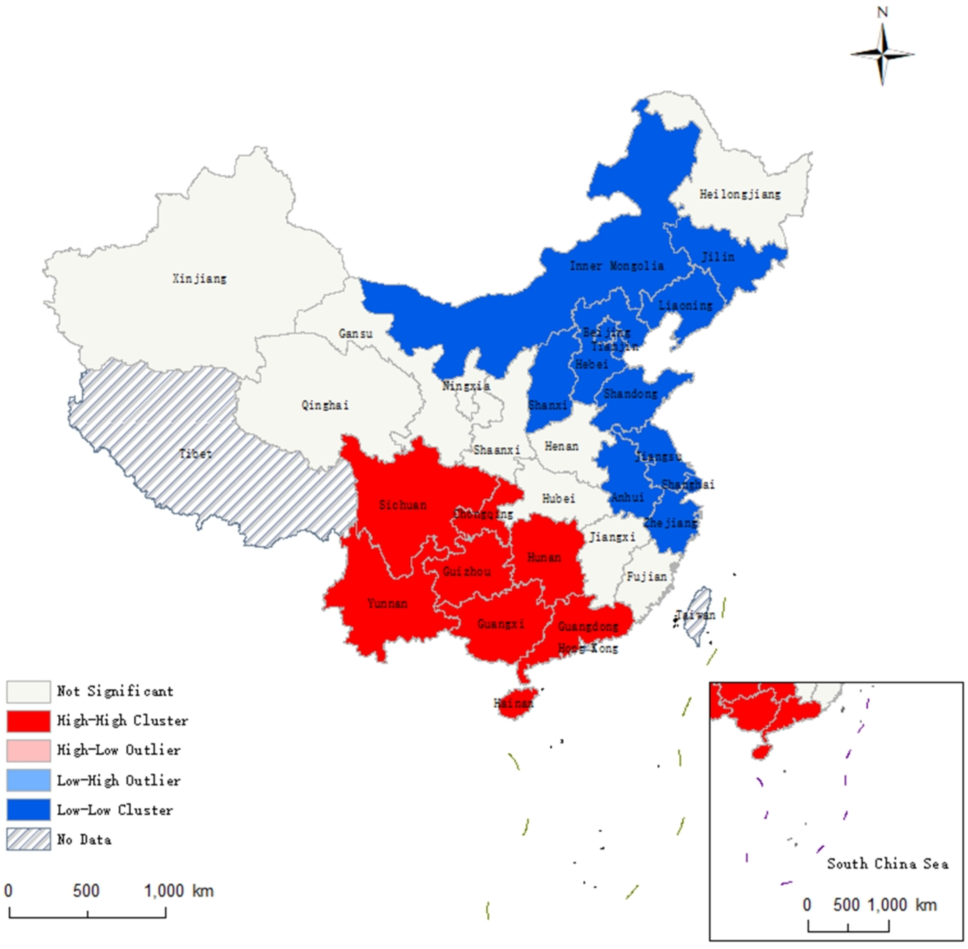

Fig.3 The results of Anselin Local Moran's I about short stature in China (2014)

206x207mm (300 x 300 DPI)

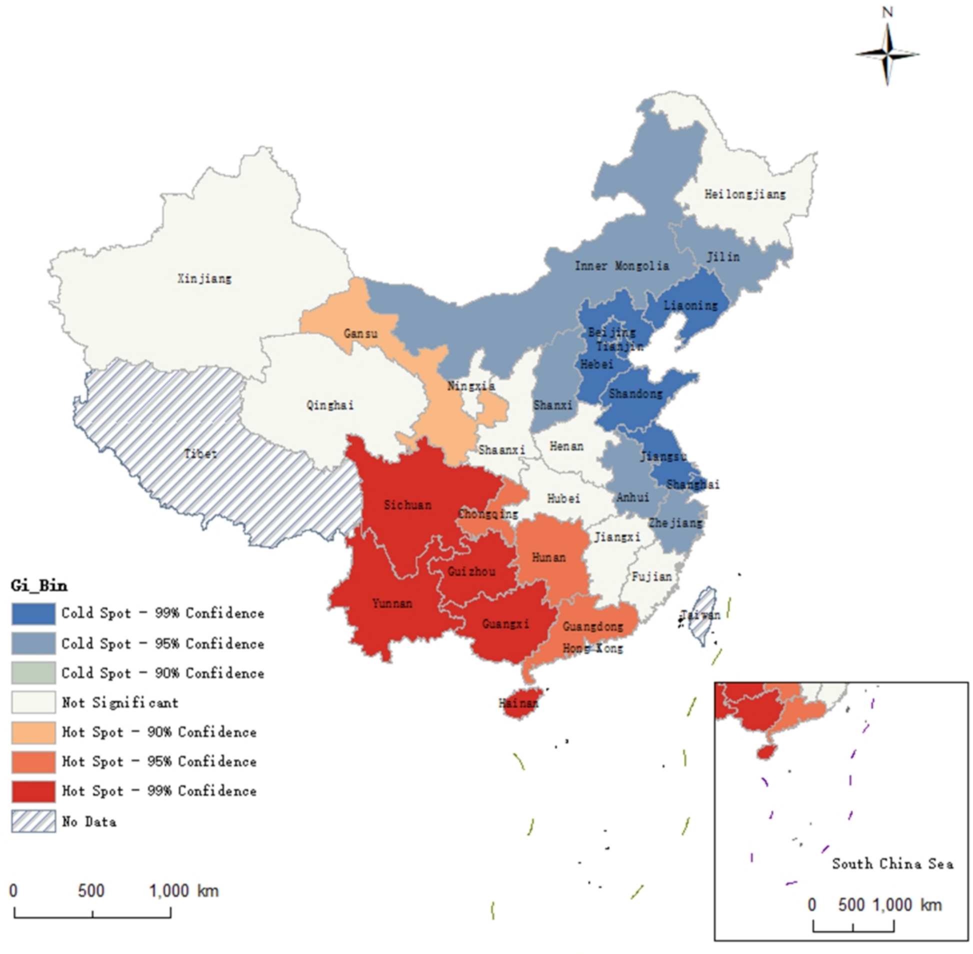

Fig.4 The result of Hotspot Getis-Ord,Gi about short stature in China (2014)

206x207mm (300 x 300 DPI)

Supplementary

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

Province	China 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

Xinjiang	4.11	4.09

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Spatial and Demographic Disparities in Short Stature among School Children Aged 7-18 Years: A Nation-Wide Survey in China, 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 $p < 0.0001$). 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

short stature in southwestern China. This provides corroborating evidence for a tailored strategy on short stature prevention and reduction in special areas.

Strengths and Limitations of This Study

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

The results provide corroborating evidence for a tailored strategy on short stature prevention and reduction in special areas.

Our study raises a discussion that, because of the geographical and climatic differences between north and south China, we may need to consider regional differences in height when we diagnose short stature.

Our study is a cross-sectional study. We did not explore the cause of short stature and did not perform a follow-up to learn the adult heights of our participants.

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 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.

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).

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^o 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]

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 indicates strong spatial dispersion, and values close to positive one indicates strong clustering (autocorrelation). Moran's I statistics with p-values less than 0.05 are considered statistically significant. Getis-Ord Gi* was proposed by Arthur Getis and Keith Ord in 1992.[22] In our study, more highly positive Gi * Z-scores indicate high short stature clustering, scores near 0 indicate no clustering existed, and negative scores suggest lower short stature clustering. Local Moran's I, proposed by Luc Anselin in 1995, estimates the association of the short stature cluster and its neighboring clusters within a specified geographical area (inter-cluster variation).[23] We used the Anselin Local Moran's I to estimate the spatial clustering of high-high clustering, low-low clustering, or mixed clustering (i.e., low near high or vice versa). Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC) and geographical disparities were analyzed by ArcMap software 10.2 (ESRI, Redlands, California, USA). p-values less than 0.05 (two-sided) were considered statistically significant.

Patient and Public Involvement

Participants were not involved in the design of this study.

Results

Characteristics of Participating Children

In total, 213,795 children, comprising 106,857 boys and 106,938 girls, were enrolled in our study. The participants were distributed evenly between sexes (i.e., the ratio of boys and girls was close to 1:1) and among the groups of different ages, urban-rural areas, and regions with different socioeconomic development levels (Table 1).

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

Variables	**N (%)**		
	Boys (**n=** 106857)	**Girls** (**n=** 106938)	**Both** (**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; $p <$

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.

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

Stratification	Prevalence, %		
	Both	Boys	Girls
	China guideline/standard		
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 guideline/standards		
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)
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 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.

Table 3 Discrepancy of genders in different residence and regions

Stratification	China reference N (%)	WHO reference N (%)

	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 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.

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 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, −2 SDS 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 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 to developed ones. Both the higher prevalence in rural areas and less developed regions indicated that children living in socioeconomically delayed areas were at a higher risk of having stunted growth. Based on the WHO growth reference of 2007, the prevalence for stunted children and adolescents in 2002 was 16.4% in rural China and 5.7% in urban China.[27] China has made tremendous economic achievements, but this economic development does not necessarily reduce inequalities in nutrition and health care services.[28] A study has shown that there have been declining trends of urban–rural disparities since China's Reform and Opening Policy was established in 1978.[29] 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 before accelerating during puberty.[30, 31] The acceleration of the rate of height growth in puberty can partly explain the differences in short stature prevalence between in different age groups. When does puberty begin in Chinese adolescents? Girls may begin puberty earlier than boys.[32] One study showed that the median age of menarche in Chinese girls was 12.47 years in 2010.[33] 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.[34] 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.[35] The timing of puberty reported by literature is consistent with our study results. The lowest point of short stature prevalence occurred in the 10–12 and 7–9 age groups for boys and girls, respectively. During these ages, Chinese boys and girls start puberty. The rate of height growth accelerated, whereas short stature prevalence 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 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 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.

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 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.

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 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.

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 short stature prevalence in different genders, regions, ages groups from CNSSCH data. Jia Ma wrote the manuscript. Fen Dong analyzed demographic characteristics of data by mathematical statistics and revised the manuscript.Tao Pei, Jie Chen, Sihui Guo analyzed spatial distribution of short stature and Tao Pei helped to revised the manuscript. Qiuling Zhao and shunan Wang helped 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 (2018-94-K68).

Data sharing statement: No additional data are available.

References

1. Smuel K, Yeshayahu Y. "Real-world" pediatric endocrine practice; how much is it influenced by physician's gender and region of practice. Results of an international survey. Journal of evaluation in clinical practice. 2017;23(4):866-9.
2. Tornese G, Pellegrin MC, Barbi E, Ventura A. Pediatric endocrinology through syndromes. European journal of medical genetics. 2019.
3. Rogol AD, Hayden GF. Etiologies and early diagnosis of short stature and growth failure in children and adolescents. The Journal of pediatrics. 2014;164(5 Suppl):S1-14.e6.
4. Murray PG, Clayton PE, Chernausek SD. A genetic approach to evaluation of short stature of undetermined cause. The lancet Diabetes & endocrinology. 2018;6(7):564-74.

5. Stewart CP, Iannotti L, Dewey KG, Michaelsen KF, Onyango AW. Contextualising complementary feeding in a broader framework for stunting prevention. Maternal & child nutrition. 2013;9 Suppl 2:27-45.

6. Allen DB, Cuttler L. Clinical practice. Short stature in childhood--challenges and choices. The New England journal of medicine. 2013;368(13):1220-8.

7. Kim B, Park MJ. The influence of weight and height status on psychological problems of elementary schoolchildren through child behavior checklist analysis. Yonsei medical journal. 2009;50(3):340-4.

8. Derraik JG, Lundgren M, Cutfield WS, Ahlsson F. Maternal Height and Preterm Birth: A Study on 192,432 Swedish Women. PloS one. 2016;11(4):e0154304.

9. Black RE, Victora CG, Walker SP, Bhutta ZA, Christian P, de Onis M, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. Lancet (London, England). 2013;382(9890):427-51.

10. Marshall WA. Geographical and ethnic variations in human growth. British medical bulletin. 1981;37(3):273-9.

11. Kinyoki DK, Kandala NB, Manda SO, Krainski ET, Fuglstad GA, Moloney GM, et al. Assessing comorbidity and correlates of wasting and stunting among children in Somalia using cross-sectional household surveys: 2007 to 2010. BMJ open. 2016;6(3):e009854.

12. Hagos S, Hailemariam D, WoldeHanna T, Lindtjorn B. Spatial heterogeneity and risk factors for stunting among children under age five in Ethiopia: A Bayesian geo-statistical model. PloS one. 2017;12(2):e0170785.

13. United Nations International Children's Emergency Fund. Malnutrition prevalences remain alarming: stunting is declining too slowly while wasting still impacts the lives of far too many young children 2018 [Available from: https://data.unicef.org/topic/nutrition/malnutrition/.

14. Cai CH, Dong B, Ma J. [District differences and regional division of heights among Chinese Han children and adolescents]. Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi. 2012;33(2):197-200.

15. So HK, Nelson EA, Sung RY, Ng PC. Implications of using World Health Organization growth reference (2007) for identifying growth problems in Hong Kong children aged 6 to 18 years. Hong Kong medical journal = Xianggang yi xue za zhi. 2011;17(3):174-9.

16. Research Group of the Physical Fitness and Health Surveillance of Chinese school students. Report on the Physical Fitness and Health Surveillance of Chinese School Students. Beijing, China.: High Education Press; 2016.

17. de Onis M, Onyango AW. WHO child growth standards. Lancet (London, England). 2008;371(9608):204.

18. Chinese Society of Pediatric Endocrinology and Metabolism. Guideline for diagnosis and treatment of short stature children. Chinese Journal of Pediatrics. 2008;46(6):20-1.

19. Li H, Ji CY, Zong XN, Zhang YQ. [Height and weight standardized growth charts for Chinese children and adolescents aged 0 to 18 years]. Zhonghua er ke za zhi = Chinese journal of pediatrics. 2009;47(7):487-92.

20. Moran PAP. Notes on continuous stochastic phenomena. Biometrika. 1950;31(1):17–23

21. Bernstein RM, Dufour DL. Special Section: Worldwide variation in human growth: 40 years later. American Journal of Human Biology the Official Journal of the Human Biology Council. 2017;29(2).

22. Getis A, Ord JK. The Analysis of Spatial Association by Use of Distance Statistics. Geographical Analysis. 2010;24(3):189-206.
23. Anselin L. Local Indicators of Spatial Association—LISA. Geographical Analysis. 1995;27(2):93-115.
24. World Health Organization. Child malnutrition [Available from: http://www.who.int/gho/health_equity/outcomes/health_equity_child_malnutrition_a.pdf.
25. Song Y, Agardh A, Ma J, Li L, Lei Y, Stafford RS, et al. National trends in stunting, thinness and overweight among Chinese school-aged children, 1985-2014. International journal of obesity (2005). 2019;43(2):402-11.
26. UNICEF WHO, World Bank Group,. Joint Child Malnutrition Estimates – Levels and Trends 2016 [Available from: http://www.who.int/nutgrowthdb/estimates2015/en/.
27. Li YP, Hu XQ, Jing Z, Yang XG, Ma GS. Application of the WHO growth reference (2007) to assess the nutritional status of children in China. Biomedical and environmental sciences : BES. 2009;22(2):130-5.
28. Hsiao WC, Liu Y. Economic reform and health--lessons from China. The New England journal of medicine. 1996;335(6):430-2.
29. Liu H, Fang H, Zhao Z. Urban-rural disparities of child health and nutritional status in China from 1989 to 2006. Economics and human biology. 2013;11(3):294-309.
30. Tanner JM, Davies PS. Clinical longitudinal standards for height and height velocity for North American children. Journal of Pediatrics. 1985;107(3):317-29.
31. Karlberg J. On the construction of the infancy-childhood-puberty growth standard. Acta paediatrica Scandinavica Supplement. 1989;356:26-37.
32. Tanner JM, Whitehouse RH, Marubini E, Resele LF. The adolescent growth spurt of boys and girls of the Harpenden growth study. Annals of human biology. 1976;3(2):109-26.
33. Yi S, Jun M, Hai-Jun W, Zhiqiang W, Peijin H, Bing Z, et al. Trends of age at menarche and association with body mass index in Chinese school-aged girls, 1985-2010. Journal of Pediatrics. 2014;165(6):1172-7.e1.
34. Ma HM, Chen SK, Chen RM, Zhu C, Xiong F, Li T, et al. Pubertal development timing in urban Chinese boys. International journal of andrology. 2011;34(5 Pt 2):e435-45.
35. Lam TH, Shi HJ, Ho LM, Stewart SM, Fan S. Timing of pubertal maturation and heterosexual behavior among Hong Kong Chinese adolescents. Archives of sexual behavior. 2002;31(4):359-66.
36. Orden AB, Apezteguia MC. Weight and height centiles of Argentinian children and adolescents: a comparison with WHO and national growth references. Annals of human biology. 2016;43(1):9-17.
37. Kulaga Z, Litwin M, Tkaczyk M, Rozdzynska A, Barwicka K, Grajda A, et al. The height-, weight-, and BMI-for-age of Polish school-aged children and adolescents relative to international and local growth references. BMC public health. 2010;10:109.
38. de Wilde JA, van Dommelen P, van Buuren S, Middelkoop BJ. Height of South Asian children in the Netherlands aged 0-20 years: secular trends and comparisons with current Asian Indian, Dutch and WHO references. Annals of human biology. 2015;42(1):38-44.
39. Osgood-Zimmerman A, Millear AI, Stubbs RW, Shields C, Pickering BV, Earl L, et al. Mapping child growth failure in Africa between 2000 and 2015. Nature. 2018;555(7694):41.

40. Brownwright TK, Zan MD, Panhuis WGV. Spatial clustering of measles vaccination coverage among children in sub-Saharan Africa. BMC public health. 2017;17(1):957.
41. Mantri S, Fullard M, Gray SL, Weintraub D, Hubbard RA, Hennessy S, et al. Patterns of Dementia Treatment and Frank Prescribing Errors in Older Adults With Parkinson Disease. JAMA neurology. 2018.
42. Kershaw KN, Robinson WR, Gordon-Larsen P, Hicken MT, Jr GD, Carnethon MR, et al. Association of Changes in Neighborhood-Level Racial Residential Segregation With Changes in Blood Pressure Among Black Adults: The CARDIA Study. Journal of the American Medical Association. 2017;177(7):996.
43. Xu X, Zhou G, Wang Y, Hu Y, Ruan Y, Fan Q, et al. Microgeographic Heterogeneity of Border Malaria During Elimination Phase, Yunnan Province, China, 2011-2013. Emerging infectious diseases. 2016;22(8):1363-70.
44. Wang A, Scherpbier RW, Huang X, Guo S, Yang Y, Josephs-Spaulding J, et al. The dietary diversity and stunting prevalence in minority children under 3 years old: a cross-sectional study in forty-two counties of Western China. The British journal of nutrition. 2017;118(10):840-8.
45. Wu L, Yang Z, Yin SA, Zhu M, Gao H. The relationship between socioeconomic development and malnutrition in children younger than 5 years in China during the period 1990 to 2010. Asia Pacific journal of clinical nutrition. 2015;24(4):665-73.
46. Pennisi E. High altitude may have driven short stature in Peruvians. Science (New York, NY). 2018;360(6390):696.
47. Tripathy V, Gupta R. Growth among Tibetans at high and low altitudes in India. American journal of human biology : the official journal of the Human Biology Council. 2007;19(6):789-800.
48. Weitz CA, Garruto RM. Stunting and the Prediction of Lung Volumes Among Tibetan Children and Adolescents at High Altitude. High altitude medicine & biology. 2015;16(4):306-17.
49. Tianyi WU, Kayser B. High Altitude Adaptation in Tibetans. High altitude medicine & biology. 2006;7(3):193.
50. Greksa LP. Growth and development of Andean high altitude residents. High altitude medicine & biology. 2006;7(2):116-24.
51. Wells JC. Environmental temperature and human growth in early life. Journal of theoretical biology. 2000;204(2):299-305.
52. Serrat MA. Environmental temperature impact on bone and cartilage growth. Comprehensive Physiology. 2014;4(2):621-55.
53. Phalkey RK, Aranda-Jan C, Marx S, Hofle B, Sauerborn R. Systematic review of current efforts to quantify the impacts of climate change on undernutrition. Proceedings of the National Academy of Sciences of the United States of America. 2015;112(33):E4522-9.
54. Haas JD, Campirano F. Interpopulation variation in height among children 7 to 18 years of age. Food and nutrition bulletin. 2006;27(4 Suppl Growth Standard):S212-23.
55. Natale V, Rajagopalan A. Worldwide variation in human growth and the World Health Organization growth standards: a systematic review. BMJ open. 2014;4(1):e003735.
56. Schonbeck Y, Talma H, van Dommelen P, Bakker B, Buitendijk SE, HiraSing RA, et al. The world's tallest nation has stopped growing taller: the height of Dutch children from 1955 to 2009. Pediatric research. 2013;73(3):371-7.

57. Ari Yuca S, Cesur Y, Kurtoglu S, Mazicioglu MM, Cimbek EA. Growth patterns of children of same geographic background reared in different environments. Journal of clinical research in pediatric endocrinology. 2014;6(4):233-7.
58. Ranke MB. Towards a consensus on the definition of idiopathic short stature. Hormone research. 1996;45 Suppl 2:64-6.
59. Wu X. From Assimilation to Autonomy: Realizing Ethnic Minority Rights in China's National Autonomous Regions. Chinese Journal of International Law. 2014;13(1):55-90.
60. Ning Li XG. Comparative research on the variation characteristics of height and growth of minority nationalities students with Han nationality aged from 7 to 18 in southwest China. Modern Preventive Medicine. 2009;36(3):445-9.
61. Yin XJ JC. Malnutrition Prevalence in Lasa Xizang Children and Adolescents. Biomedical and environmental sciences : BES. 2014;27(8):614-26.

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.

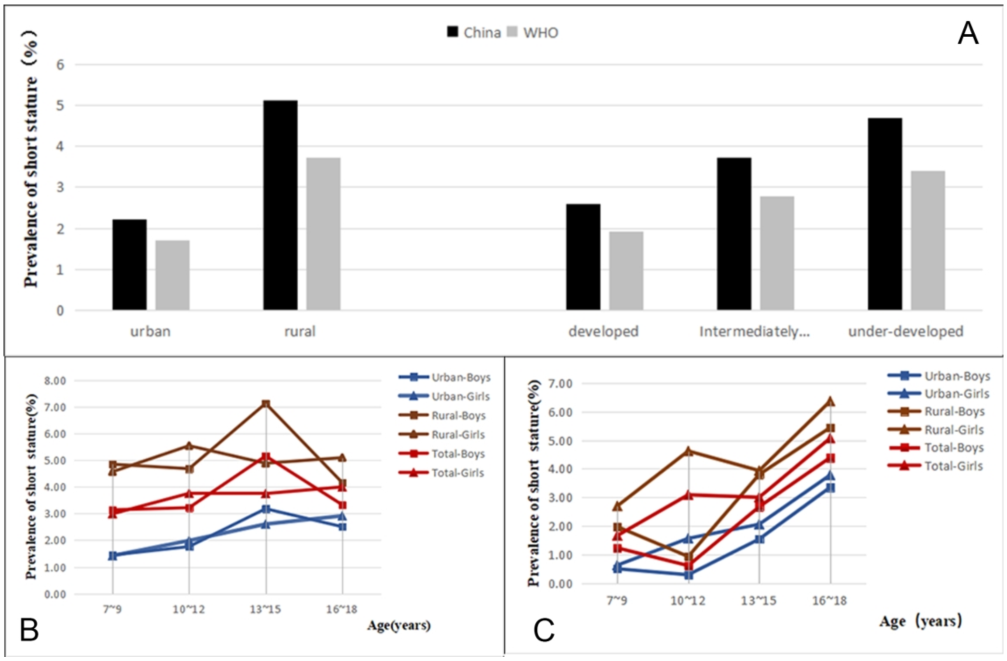
B. The distribution of short stature standardized prevalence according WHO growth reference.

C. The results of Anselin Local Moran's I about short stature according China growth reference.

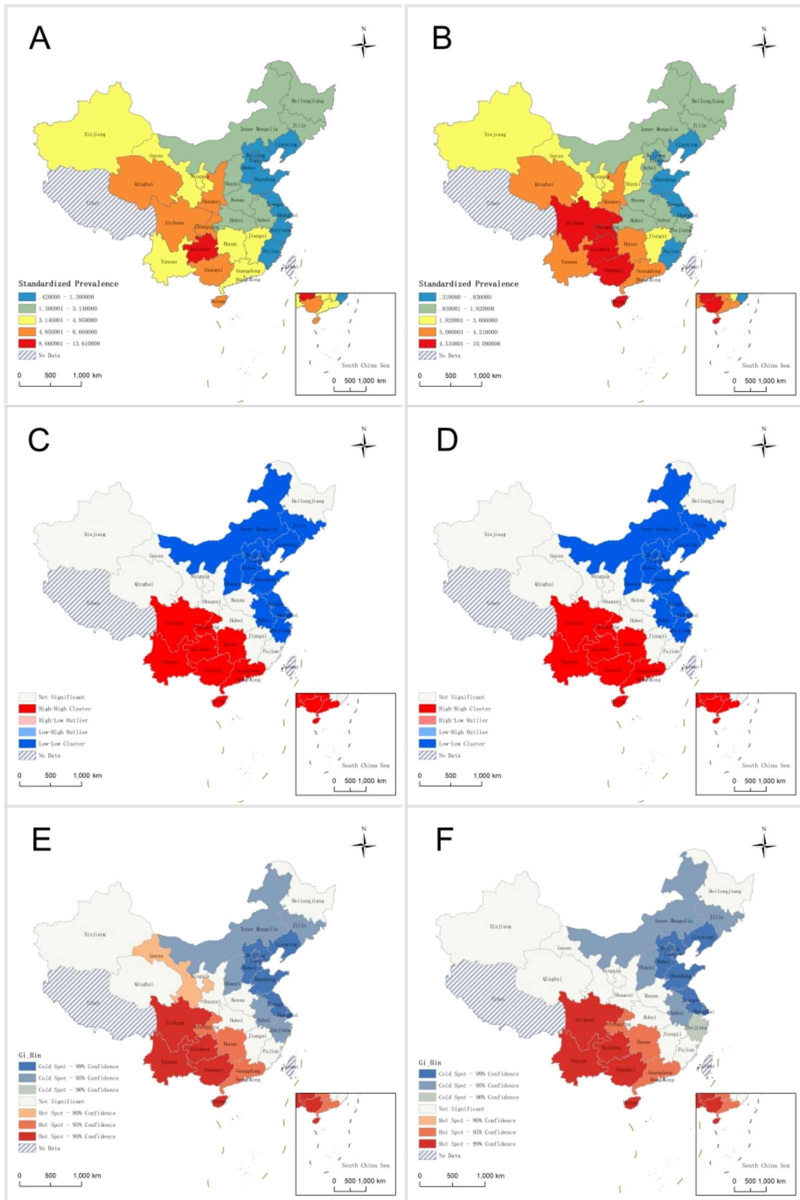
D. The results of Anselin Local Moran's I about short stature according WHO growth reference.

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.



A.The distribution of short stature standardized prevalence according China growth reference.
B.The distribution of short stature standardized prevalence according WHO growth reference.
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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 reference		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

Table 2 The results of Anselin Local Moran's I

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

Table3 The results of Hotspot Getis-Ord, Gi*

Province	China 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

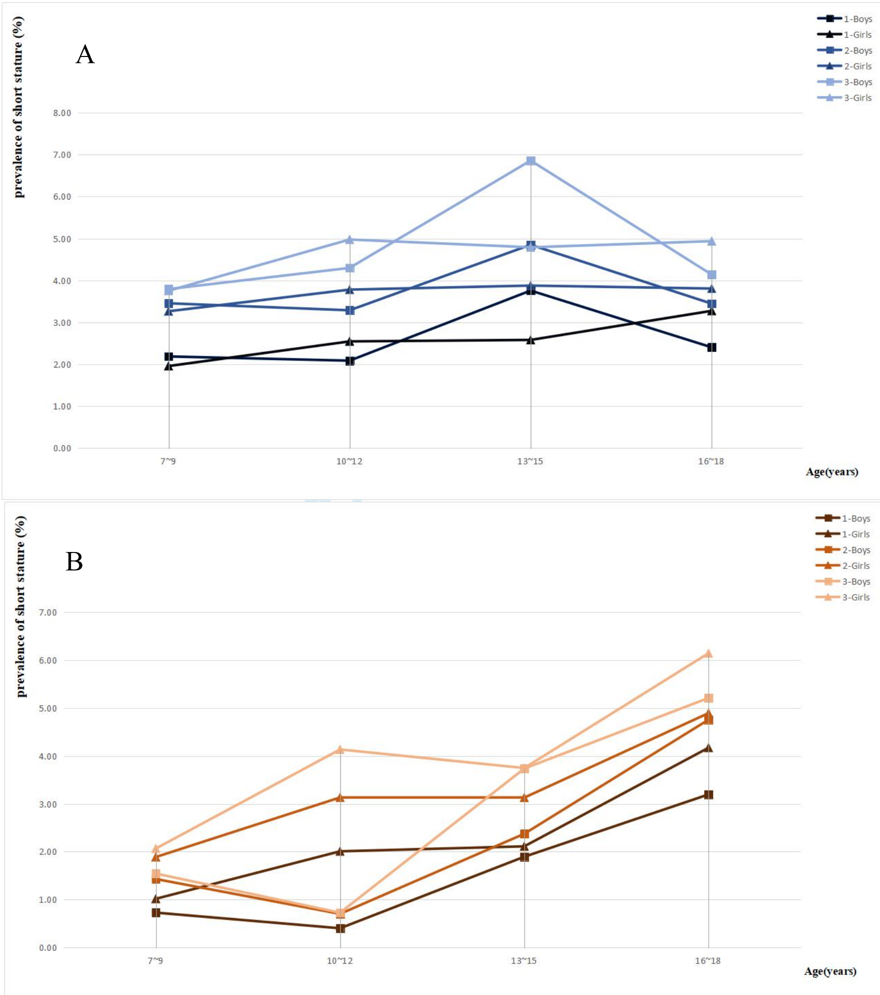

Figure 1 The discrepancy of prevalence between different age groups in different regions.

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.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract		Line 5
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found		Line2-4 Line26-27
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported		Line1-27
Objectives	3	State specific objectives, including any prespecified hypotheses		Line5-7
Methods				
Study design	4	Present key elements of study design early in the paper		Line14-15
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		Line16-27
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—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 *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants		Line16-23

		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	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	Line8-13
Bias	9	Describe any efforts to address potential sources of bias	Line26-27
Study size	10	Explain how the study size was arrived at	Line21-24

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Line18-27
		(*b*) Describe any methods used to examine subgroups and interactions	Line22
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Line20-22
		(*e*) Describe any sensitivity analyses	
Results			
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	Line19
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Line19-22
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	

		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures	9	Line4-5
Main results	16	(*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 included	10	Line5-7
		(*b*) Report category boundaries when continuous variables were categorized	10	Line11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12	Line15-20
Discussion				
Key results	18	Summarise key results with reference to study objectives	13	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		
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		Line14-27
Generalisability	21	Discuss the generalisability (external validity) of the study results		Line9-17
Other information				
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	20	Line8-10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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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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Spatial and Demographic Disparities in Short Stature among School Children 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 $p < 0.0001$). 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

stature in southwestern China. This provides corroborating evidence for a tailored strategy on short stature prevention and reduction in special areas.

Strengths and Limitations of This Study

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

The results provide corroborating evidence for a tailored strategy on short stature prevention and reduction in special areas.

Our study raises a discussion that, because of the geographical and climatic differences between north and south China, we may need to consider regional differences in height when we diagnose short stature.

Our study is a cross-sectional study. We did not explore the cause of short stature and did not perform a follow-up to learn the adult heights of our participants.

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.

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).

Anthropometric Measurements

Standing height (cm) was measured by trained staff following a standardized procedure, which was in accordance with the anthropometry methods in the 2006 World Health Organization (WHO) Child Growth Reference.[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^{o} 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]

Statistical Analysis

The demographic disparities of short stature were presented as a number (percent). Prevalence was age-standardized (or age-gender-standardized) directly to the China 2000 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 prevalence of short stature 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 proposed by Patrick Alfred Pierce Moran in 1950, to measure spatial autocorrelation.[20 21] Moran's I ranges from −1 to 1.[22] Values approach to zero means lacking a spatial association (i.e., a random distribution), values approach to negative one means spatial dispersion, and values approach to positive one means clustering.[22]

Moran's I statistics with p-values less than 0.05 are considered statistically significant. Getis-Ord Gi* was proposed by Arthur Getis and Keith Ord in 1992.[23] In our study, positive Gi * Z-scores indicate high short stature clustering, scores near 0 indicate no clustering existed, and negative scores suggest lower short stature clustering. Local Moran's I, proposed by Luc Anselin in 1995, estimates inter-cluster variation.[24] We used the Anselin Local Moran's I to estimate the spatial clustering of high-high clustering, low-low clustering, low-high clustering and high-low clustering.[22] Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC) and geographical disparities were analyzed by ArcMap software 10.2 (ESRI, Redlands, California, USA). p-values less than 0.05 (two-sided) were considered statistically significant.

Patient and Public Involvement

Participants were not involved in the design of this study.

Results

Characteristics of Participating Children

In total, 213,795 children, comprising 106,857 boys and 106,938 girls, were enrolled in our study. The participants were distributed evenly between sexes (i.e., the ratio of boys and girls was close to 1:1) and among the groups of different ages, urban-rural areas, and regions with different socioeconomic development levels (table 1).

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

Variables	N (%)		
	Boys (n= 106857)	**Girls (n= 106938)**	**Both (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; $p < 0.0001$) 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 was 3.70 and 2.69% according to the Chinese and WHO growth references, respectively. Notedly, the prevalence of short stature defined by the Chinese reference was higher than that based on the WHO reference.

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

Stratification	Prevalence, %		
	Both	Boys	Girls
China reference			
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			
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)

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 overall prevalence of short stature according to the Chinese growth reference ($p = 0.260$). However, we observed this difference in prevalence evaluated by the WHO growth reference ($p < 0.0001$). Because we found significant differences of prevalence of short stature 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 prevalence of short stature 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.

Table 3 Discrepancy of genders in different residence and regions

Stratification	China reference		WHO reference	
	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 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.

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, 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 Chongqing, 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 reference, which is lower than our result. This difference could be partly attributed to the different SD adopted in our study. We used the third centile (−1.88 SD) to define short stature, which is currently routine clinical practice in China. In Song's study, −2 SD was used to assess stunting, which may have contributed to 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%.[26] 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 was 36.2, 35.2, 15.8, 14.4, 10.1, and 9.2%, respectively.[27] 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. The prevalence of short stature helps us to know the nutritional and pathological condition of children and provide useful data to decision makers .

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 to developed ones. Both the higher prevalence in rural areas and less developed regions indicated that children living in socioeconomically delayed areas were at a higher risk of having stunted growth. Based on the WHO growth reference, the prevalence of stunting in children was 16.4% and 5.7% in rural and urban China respectively in 2002.[28] Economic development of China does not reduce inequalities in nutrition and health care services.[29] A study has shown that there have been declining trends of urban–rural 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 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, 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 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 places[48]. 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.

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).

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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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 prevalence of short stature in different genders, regions, ages groups from CNSSCH data. Jia Ma wrote the manuscript. Fen Dong analyzed demographic characteristics of data by mathematical statistics and revised the manuscript.Tao Pei, Jie Chen, Sihui Guo analyzed spatial distribution of prevalence of short stature and Tao Pei helped to revised the manuscript. Qiuling Zhao and Shunan Wang helped to apply the research fund and check the data. All authors have contributed to the work and approved the manuscript.

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Ethics approval: Informed consent was obtained from both parents and schoolchildren 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 (2018-94-K68).

Data sharing statement: No additional data are available.

References

1. Smuel K, Yeshayahu Y. "Real-world" pediatric endocrine practice; how much is it influenced by physician's gender and region of practice. Results of an international survey. *Journal of evaluation in clinical practice* 2017;23(4):866-69. doi: 10.1111/jep.12745 [published Online First: 2017/06/07]
2. Tornese G, Pellegrin MC, Barbi E, et al. Pediatric endocrinology through syndromes. *European journal of medical genetics* 2019 doi: 10.1016/j.ejmg.2019.01.004 [published Online First: 2019/01/18]
3. Rogol AD, Hayden GF. Etiologies and early diagnosis of short stature and growth failure in children and adolescents. *The Journal of pediatrics* 2014;164(5 Suppl):S1-14.e6. doi: 10.1016/j.jpeds.2014.02.027 [published Online First: 2014/04/16]
4. Murray PG, Clayton PE, Chernausek SD. A genetic approach to evaluation of short stature of undetermined cause. *The lancet Diabetes & endocrinology* 2018;6(7):564-74. doi: 10.1016/s2213-8587(18)30034-2 [published Online First: 2018/02/06]
5. Stewart CP, Iannotti L, Dewey KG, et al. Contextualising complementary feeding in a broader framework for stunting prevention. *Maternal & child nutrition* 2013;9 Suppl 2:27-45. doi: 10.1111/mcn.12088 [published Online First: 2013/10/23]

6. Allen DB, Cuttler L. Clinical practice. Short stature in childhood--challenges and choices. *The New England journal of medicine* 2013;368(13):1220-8. doi: 10.1056/NEJMcp1213178 [published Online First: 2013/03/29]

7. Kim B, Park MJ. The influence of weight and height status on psychological problems of elementary schoolchildren through child behavior checklist analysis. *Yonsei medical journal* 2009;50(3):340-4. doi: 10.3349/ymj.2009.50.3.340 [published Online First: 2009/07/02]

8. Derraik JG, Lundgren M, Cutfield WS, et al. Maternal Height and Preterm Birth: A Study on 192,432 Swedish Women. *PloS one* 2016;11(4):e0154304. doi: 10.1371/journal.pone.0154304 [published Online First: 2016/04/23]

9. Black RE, Victora CG, Walker SP, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet (London, England)* 2013;382(9890):427-51. doi: 10.1016/s0140-6736(13)60937-x [published Online First: 2013/06/12]

10. Marshall WA. Geographical and ethnic variations in human growth. *British medical bulletin* 1981;37(3):273-9. [published Online First: 1981/09/01]

11. Kinyoki DK, Kandala NB, Manda SO, et al. Assessing comorbidity and correlates of wasting and stunting among children in Somalia using cross-sectional household surveys: 2007 to 2010. *BMJ open* 2016;6(3):e009854. doi: 10.1136/bmjopen-2015-009854 [published Online First: 2016/03/11]

12. Hagos S, Hailemariam D, WoldeHanna T, et al. Spatial heterogeneity and risk factors for stunting among children under age five in Ethiopia: A Bayesian geo-statistical model. *PloS one* 2017;12(2):e0170785. doi: 10.1371/journal.pone.0170785 [published Online First: 2017/02/09]

13. United Nations International Children's Emergency Fund. Malnutrition prevalences remain alarming: stunting is declining too slowly while wasting still impacts the lives of far too many young children 2018 [Available from: https://data.unicef.org/topic/nutrition/malnutrition/.

14. Cai CH, Dong B, Ma J. [District differences and regional division of heights among Chinese Han children and adolescents]. *Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi* 2012;33(2):197-200.

15. So HK, Nelson EA, Sung RY, et al. Implications of using World Health Organization growth reference (2007) for identifying growth problems in Hong Kong children aged 6 to 18 years. *Hong Kong medical journal = Xianggang yi xue za zhi* 2011;17(3):174-9. [published Online First: 2011/06/04]

16. Research Group of the Physical Fitness and Health Surveillance of Chinese school students. Report on the Physical Fitness and Health Surveillance of Chinese School Students. Beijing, China.: High Education Press 2016.

17. de Onis M, Onyango AW. WHO child growth standards. *Lancet (London, England)* 2008;371(9608):204. doi: 10.1016/s0140-6736(08)60131-2 [published Online First: 2008/01/22]

18. Chinese Society of Pediatric Endocrinology and Metabolism. Guideline for diagnosis and treatment of short stature children. *Chinese Journal of Pediatrics* 2008;46(6):20-21.

19. Li H, Ji CY, Zong XN, et al. [Height and weight standardized growth charts for Chinese children and adolescents aged 0 to 18 years]. *Zhonghua er ke za zhi = Chinese journal of pediatrics* 2009;47(7):487-92. [published Online First: 2009/12/03]

20. Moran PAP. Notes on continuous stochastic phenomena. *Biometrika* 1950;31(1):17–23

21. Bernstein RM, Dufour DL. Special Section: Worldwide variation in human growth: 40 years later. *American Journal of Human Biology the Official Journal of the Human Biology Council* 2017;29(2)

22. Brownwright TK, Zan MD, Panhuis WGV. Spatial clustering of measles vaccination coverage among children in sub-Saharan Africa. *BMC public health* 2017;17(1):957.

23. Getis A, Ord JK. The Analysis of Spatial Association by Use of Distance Statistics. *Geographical Analysis* 2010;24(3):189-206.

24. Anselin L. Local Indicators of Spatial Association—LISA. *Geographical Analysis* 1995;27(2):93-115.

25. World Health Organization. Child malnutrition [Available from: http://www.who.int/gho/health_equity/outcomes/health_equity_child_malnutrition_a.pdf.

26. Song Y, Agardh A, Ma J, et al. National trends in stunting, thinness and overweight among Chinese school-aged children, 1985-2014. *International journal of obesity (2005)* 2019;43(2):402-11. doi: 10.1038/s41366-018-0129-7 [published Online First: 2018/06/20]

27. UNICEF WHO, World Bank Group,. Joint Child Malnutrition Estimates – Levels and Trends 2016 [Available from: http://www.who.int/nutgrowthdb/estimates2015/en/.

28. Li YP, Hu XQ, Jing Z, et al. Application of the WHO growth reference (2007) to assess the nutritional status of children in China. *Biomedical and environmental sciences : BES* 2009;22(2):130-5. doi: 10.1016/s0895-3988(09)60035-0 [published Online First: 2009/07/22]

29. Hsiao WC, Liu Y. Economic reform and health--lessons from China. *The New England journal of medicine* 1996;335(6):430-2. doi: 10.1056/nejm199608083350611 [published Online First: 1996/08/08]

30. Liu H, Fang H, Zhao Z. Urban-rural disparities of child health and nutritional status in China from 1989 to 2006. *Economics and human biology* 2013;11(3):294-309. doi: 10.1016/j.ehb.2012.04.010 [published Online First: 2012/05/23]

31. Tanner JM, Davies PS. Clinical longitudinal standards for height and height velocity for North American children. *Journal of Pediatrics* 1985;107(3):317-29.

32. Karlberg J. On the construction of the infancy-childhood-puberty growth standard. *Acta paediatrica Scandinavica Supplement* 1989;356:26-37. [published Online First: 1989/01/01]

33. Tanner JM, Whitehouse RH, Marubini E, et al. The adolescent growth spurt of boys and girls of the Harpenden growth study. *Annals of human biology* 1976;3(2):109-26. [published Online First: 1976/03/01]

34. Yi S, Jun M, Hai-Jun W, et al. Trends of age at menarche and association with body mass index in Chinese school-aged girls, 1985-2010. *Journal of Pediatrics* 2014;165(6):1172-77.e1.

35. Ma HM, Chen SK, Chen RM, et al. Pubertal development timing in urban Chinese boys. *International journal of andrology* 2011;34(5 Pt 2):e435-45. doi: 10.1111/j.1365-2605.2011.01173.x [published Online First: 2011/06/11]

36. Lam TH, Shi HJ, Ho LM, et al. Timing of pubertal maturation and heterosexual behavior among Hong Kong Chinese adolescents. *Archives of sexual behavior* 2002;31(4):359-66. [published Online First: 2002/08/22]

37. Orden AB, Apezteguia MC. Weight and height centiles of Argentinian children and adolescents: a comparison with WHO and national growth references. *Annals of human biology* 2016;43(1):9-17. doi: 10.3109/03014460.2014.970576 [published Online First: 2014/10/29]

38. Kulaga Z, Litwin M, Tkaczyk M, et al. The height-, weight-, and BMI-for-age of Polish school-aged children and adolescents relative to international and local growth references. *BMC public health* 2010;10:109. doi: 10.1186/1471-2458-10-109 [published Online First: 2010/03/05]

39. de Wilde JA, van Dommelen P, van Buuren S, et al. Height of South Asian children in the Netherlands aged 0-20 years: secular trends and comparisons with current Asian Indian, Dutch and WHO references. *Annals of human biology* 2015;42(1):38-44. doi: 10.3109/03014460.2014.926988 [published Online First: 2014/06/26]

40. Osgood-Zimmerman A, Millear AI, Stubbs RW, et al. Mapping child growth failure in Africa between 2000 and 2015. *Nature* 2018;555(7694):41.

41. Mantri S, Fullard M, Gray SL, et al. Patterns of Dementia Treatment and Frank Prescribing Errors in Older Adults With Parkinson Disease. *JAMA neurology* 2018 doi: 10.1001/jamaneurol.2018.2820 [published Online First: 2018/10/05]

42. Kershaw KN, Robinson WR, Gordon-Larsen P, et al. Association of Changes in Neighborhood-Level Racial Residential Segregation With Changes in Blood Pressure Among Black Adults: The CARDIA Study. *Journal of the American Medical Association* 2017;177(7):996.

43. Xu X, Zhou G, Wang Y, et al. Microgeographic Heterogeneity of Border Malaria During Elimination Phase, Yunnan Province, China, 2011-2013. *Emerging infectious diseases* 2016;22(8):1363-70.

44. Wang A, Scherpbier RW, Huang X, et al. The dietary diversity and stunting prevalence in minority children under 3 years old: a cross-sectional study in forty-two counties of Western China. *The British journal of nutrition* 2017;118(10):840-48. doi: 10.1017/s0007114517002720 [published Online First: 2017/12/01]

45. Wu L, Yang Z, Yin SA, et al. The relationship between socioeconomic development and malnutrition in children younger than 5 years in China during the period 1990 to 2010. *Asia Pacific journal of clinical nutrition* 2015;24(4):665-73. doi: 10.6133/apjcn.2015.24.4.24 [published Online First: 2015/12/24]

46. Pennisi E. High altitude may have driven short stature in Peruvians. *Science (New York, NY)* 2018;360(6390):696. doi: 10.1126/science.360.6390.696 [published Online First: 2018/05/19]

47. Tripathy V, Gupta R. Growth among Tibetans at high and low altitudes in India. *American journal of human biology : the official journal of the Human Biology Council* 2007;19(6):789-800. doi: 10.1002/ajhb.20638 [published Online First: 2007/08/11]

48. Weitz CA, Garruto RM. Stunting and the Prediction of Lung Volumes Among Tibetan Children and Adolescents at High Altitude. *High altitude medicine & biology* 2015;16(4):306-17. doi: 10.1089/ham.2015.0036 [published Online First: 2015/09/24]

49. Tianyi WU, Kayser B. High Altitude Adaptation in Tibetans. *High altitude medicine & biology* 2006;7(3):193.

50. Greksa LP. Growth and development of Andean high altitude residents. *High altitude medicine & biology* 2006;7(2):116-24. doi: 10.1089/ham.2006.7.116 [published Online First: 2006/06/13]

51. Wells JC. Environmental temperature and human growth in early life. *Journal of theoretical biology* 2000;204(2):299-305. doi: 10.1006/jtbi.2000.2015 [published Online First: 2000/07/11]

52. Serrat MA. Environmental temperature impact on bone and cartilage growth. *Comprehensive Physiology* 2014;4(2):621-55. doi: 10.1002/cphy.c130023 [published Online First: 2014/04/10]

53. Phalkey RK, Aranda-Jan C, Marx S, et al. Systematic review of current efforts to quantify the impacts of climate change on undernutrition. *Proceedings of the National Academy of Sciences of the United States of America* 2015;112(33):E4522-9. doi: 10.1073/pnas.1409769112 [published Online First: 2015/07/29]

54. Natale V, Rajagopalan A. Worldwide variation in human growth and the World Health Organization growth standards: a systematic review. *BMJ open* 2014;4(1):e003735. doi: 10.1136/bmjopen-2013-003735 [published Online First: 2014/01/10]

55. Haas JD, Campirano F. Interpopulation variation in height among children 7 to 18 years of age. *Food and nutrition bulletin* 2006;27(4 Suppl Growth Standard):S212-23. doi: 10.1177/15648265060274s505 [published Online First: 2007/03/17]

56. Schonbeck Y, Talma H, van Dommelen P, et al. The world's tallest nation has stopped growing taller: the height of Dutch children from 1955 to 2009. *Pediatric research* 2013;73(3):371-7. doi: 10.1038/pr.2012.189 [published Online First: 2012/12/12]

57. Ari Yuca S, Cesur Y, Kurtoglu S, et al. Growth patterns of children of same geographic background reared in different environments. *Journal of clinical research in pediatric endocrinology* 2014;6(4):233-7. doi: 10.4274/Jcrpe.1612 [published Online First: 2014/12/30]

58. Ranke MB. Towards a consensus on the definition of idiopathic short stature. *Hormone research* 1996;45 Suppl 2:64-6. doi: 10.1159/000184851 [published Online First: 1996/01/01]

59. Wu X. From Assimilation to Autonomy: Realizing Ethnic Minority Rights in China's National Autonomous Regions. *Chinese Journal of International Law* 2014;13(1):55-90.

60. Ning Li XG. Comparative research on the variation characteristics of height and growth of minority nationalities students with Han nationality aged from 7 to 18 in southwest China. *Modern Preventive Medicine* 2009;36(3):445-49.

61. Yin XJ JC. Malnutrition Prevalence in Lasa Xizang Children and Adolescents. *Biomedical and environmental sciences : BES* 2014;27(8):614-26.

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 standardized prevalence according China growth reference.

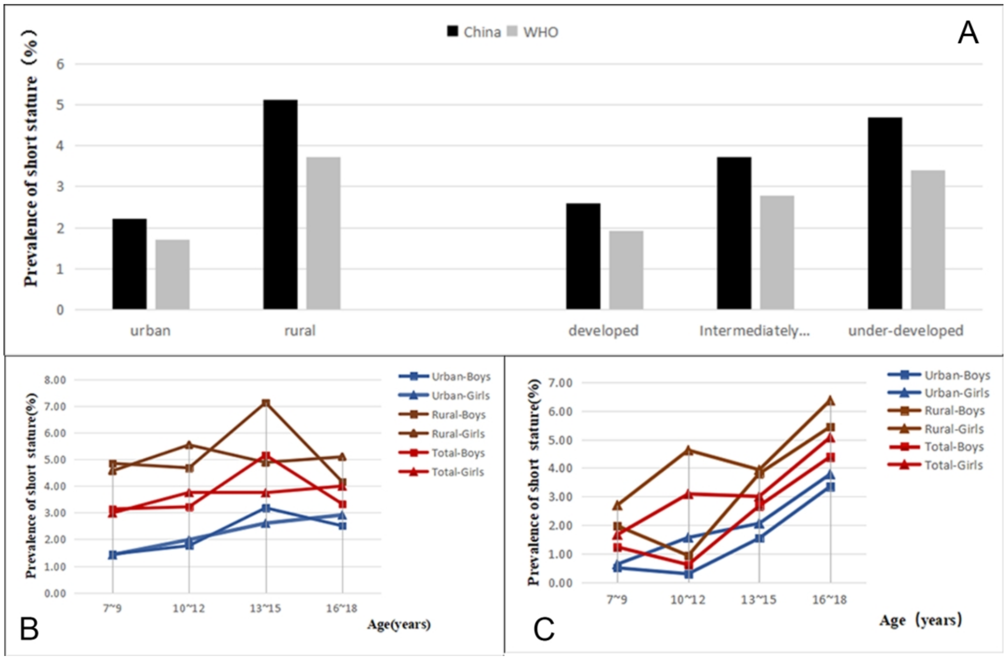
B. The distribution of standardized prevalence according WHO growth reference.

C. The results of Anselin Local Moran's I about standardized prevalence according China growth reference.

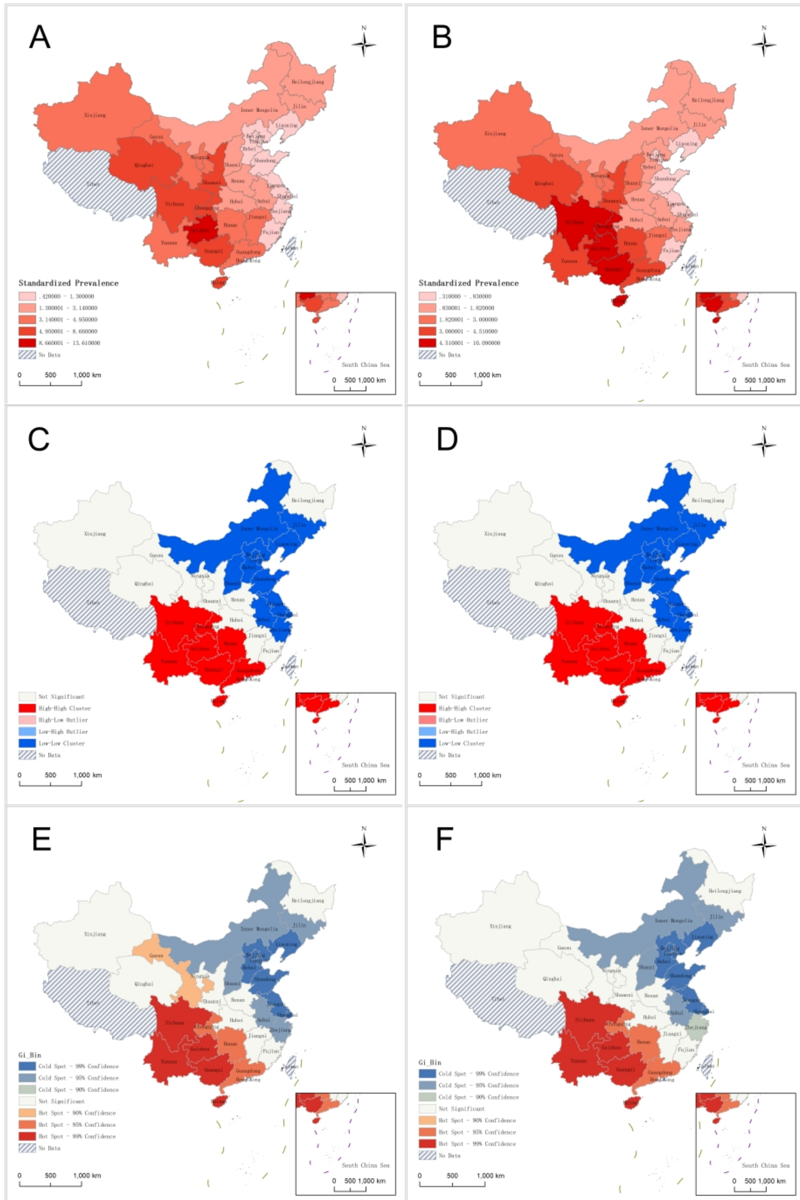
D. The results of Anselin Local Moran's I about standardized prevalence according WHO growth reference.

E. The result of Hotspot Getis-Ord, Gi* about standardized prevalence according China growth reference.

F. The result of Hotspot Getis-Ord, Gi* about standardized prevalence 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.


A
Standardized Prevalence
.420000 - 1.300000
1.300001 - 3.140000
3.140001 - 4.950000
4.950001 - 8.660000
8.660001 - 13.610000
No Data
0 500 1,000 km
South China Sea
B
Standardized Prevalence
.310000 - .830000
.830001 - 1.820000
1.820001 - 3.000000
3.000001 - 4.510000
4.510001 - 10.090000
No Data
0 500 1,000 km
South China Sea
C
Not Significant
High-High Cluster
High-Low Outlier
Low-High Outlier
Low-Low Cluster
No Data
0 500 1,000 km
South China Sea
D
E
Gi_Bin
Cold Spot - 99% Confidence
Cold Spot - 95% Confidence
Cold Spot - 90% Confidence
Not Significant
Hot Spot - 90% Confidence
Hot Spot - 95% Confidence
Hot Spot - 99% Confidence
No Data
0 500 1,000 km
South China Sea
F

Supplementary

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

Province	China reference		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 2 The results of Anselin Local Moran's I

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

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.

Table 3 The results of Hotspot Getis-Ord, Gi*

Province	China 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

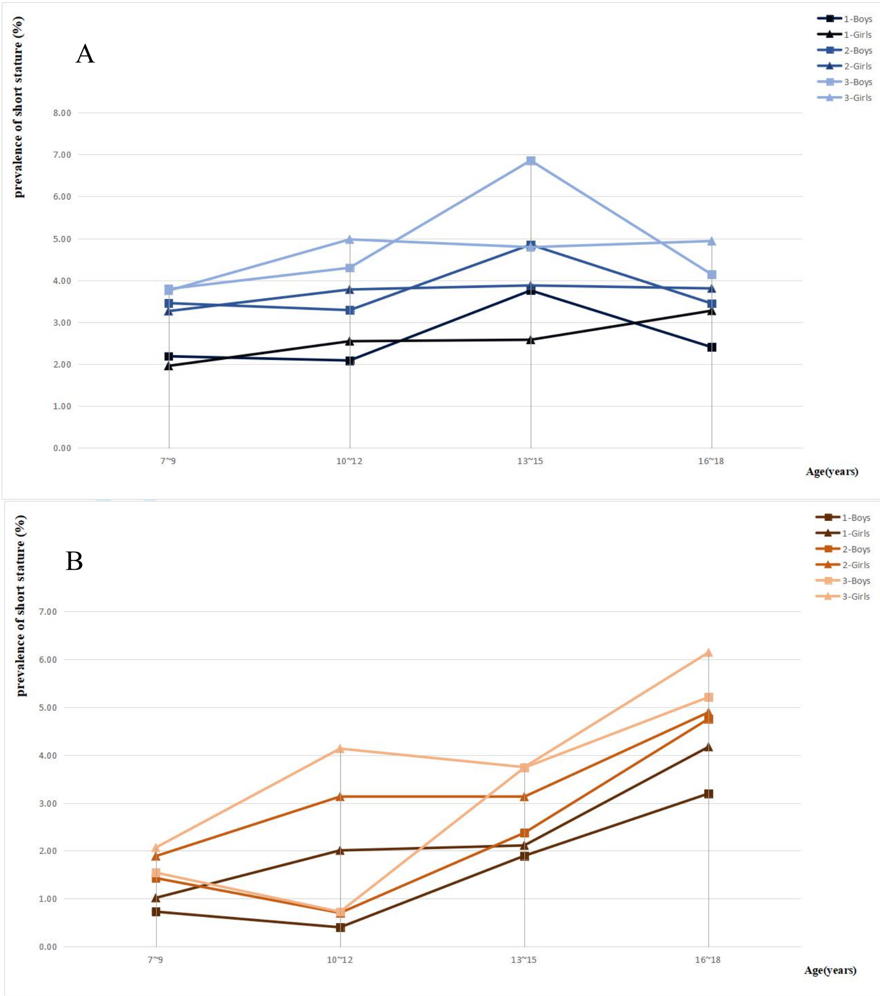


Figure 1 The discrepancy of prevalence between different age groups in different regions.

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.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract		Line 5
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found		Line2-4 Line26-27
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported		Line1-27
Objectives	3	State specific objectives, including any prespecified hypotheses		Line5-7
Methods				
Study design	4	Present key elements of study design early in the paper		Line14-15
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		Line16-27
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—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 *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants		Line16-23

		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	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	Line8-13
Bias	9	Describe any efforts to address potential sources of bias	Line26-27
Study size	10	Explain how the study size was arrived at	Line21-24

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Line18-27
		(*b*) Describe any methods used to examine subgroups and interactions	Line22
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Line20-22
		(*e*) Describe any sensitivity analyses	
Results			
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	Line19
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Line19-22
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	

		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures	9	Line4-5
Main results	16	(*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 included	10	Line5-7
		(*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		

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12	Line15-20
Discussion				
Key results	18	Summarise key results with reference to study objectives	13	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		
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		Line14-27
Generalisability	21	Discuss the generalisability (external validity) of the study results		Line9-17
Other information				
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	20	Line8-10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.