

## Preplanned Studies

## Spatial-Temporal Analysis of Drinking Water Type of Endemic Fluorosis — China, 2009–2022

Lijun Zhao<sup>1,2</sup>; Zhe Li<sup>1,2</sup>; Mang Li<sup>1,2</sup>; Hongna Sun<sup>1,2</sup>; Wei Wei<sup>1,2</sup>; Lin Gao<sup>1,2</sup>; Qiaoshi Zhao<sup>1,2</sup>; Yang Liu<sup>1,2</sup>; Xiaohong Ji<sup>1,2</sup>; Cheng Li<sup>1,2</sup>; Jian Wang<sup>1,2</sup>; Yanhui Gao<sup>1,2</sup>; Junrui Pei<sup>1,2,\*</sup>

### Summary

#### What is already known about this topic?

Endemic fluorosis, caused by high fluoride levels in drinking water, has been a significant health issue in rural areas of China for many decades.

#### What is added by this report?

There has been a notable decline in the detection rate of dental fluorosis in children aged 8–12 years in drinking water fluorosis areas across the country from 2009 to 2022. While 14 provincial-level administrative divisions are classified as low-probability clusters, Tianjin remains classified as a high-probability cluster.

#### What are the implications for public health practice?

The current policy for preventing and controlling endemic fluorosis in China needs adjustment. Rather than focusing solely on regions with high incidence, there should be a shift towards monitoring and early warning of fluoride exposure. Additionally, local containment measures should be intensified.

Drinking water type of endemic fluorosis, also known as drinking water fluorosis, is a chronic condition that occurs when individuals consume high-fluoride water over an extended period. This leads to the development of dental and skeletal fluorosis (1). Drinking water fluorosis is a global issue, affecting over 60 countries and regions. It poses a significant public health concern in 25 countries, impacting approximately 200 million individuals (2). In China, drinking water fluorosis is a prevalent form of endemic fluorosis, affecting 28 provincial-level administrative divisions (PLADs) and more than 70,000 villages (3). It is an urgent public health problem, particularly in rural areas. Over the past twenty years, rural safe water projects have been implemented by central and local governments to prevent and control drinking water fluorosis. However, there is limited information regarding the national-level temporal and spatial distribution of this disease in recent years. Therefore,

our study aimed to investigate the prevalence of dental fluorosis in drinking water fluorosis areas in China from 2009 to 2022. We found a significant decrease in the detection rate of dental fluorosis in children aged 8–12 years nationwide. Additionally, 14 PLADs were classified as low probability clusters, while Tianjin remained a high probability cluster. These findings provide valuable insights for national adjustments to drinking water fluorosis prevention and control strategies.

The study data were obtained from the Surveillance Report of the Endemic Disease Control Center of the China CDC. The data collected spanned from 2009 to 2022 and focused on the detection rate of dental fluorosis in children aged 8–12 years in 27 PLADs of China, with the exception of Xizang.

We used an Autoregressive Integrated Moving Average (ARIMA) model to analyze national children's dental fluorosis detection rates from 2009–2018. The ARIMA model was constructed using the Augmented Dickey-Fuller test with the Stats package in R [version 4.3.1; R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria] to assess the effectiveness of prevention and control measures. We analyzed the smoothness of the logit-transformed detection rate and the residuals of the model were tested with the Ljung-Box model ( $P > 0.05$ ) to determine white noise. The Bayesian information criterion (BIC) was used to select the best model fit.

Additionally, we performed spatial analysis on the detection rates of dental fluorosis in children from 2009 to 2022 to examine geographic aggregation. The Local indicators of spatial autocorrelation (LISA) analysis was conducted using GeoDa (version 1.20.0; GeoDa Institute) software to calculate global and local Moran's indices (Moran's I value).

Finally, the space-time interaction of dental fluorosis detection rates among children in each province from 2009 to 2022 was analyzed using SaTScan (version 10.1; GeoDa Institute). A moving scanning window

method was employed, with a circular window at the bottom varying in radius from 0 to 50% of the total population, and the log-likelihood ratio (LLR) was used as the statistic. A higher LLR indicated a higher likelihood of an area being an agglomeration area. The odds ratio (*OR*) for the area was then calculated and tested for statistical significance using the Global Space-Time Interaction Tests, with a test level of  $\alpha = 0.05$ .

From 2009 to 2022, the prevalence of dental fluorosis among children aged 8–12 years in areas of China with endemic fluorosis of drinking water showed a consistent decrease. The detection rate decreased from 34.87% in 2009 to 10.19% in 2022 (Table 1). In China, the control standard for endemic fluorosis areas sets a target detection rate of less than 30% in children aged 8–12 years. Additionally, a limit of 15% is used for the assessment of eliminating coal-burning type of endemic fluorosis. In 2013, the detection rate fell below 30% for the first time, and in 2020 it fell below 15%. The monitoring data for the detection rate of children's dental fluorosis aligned closely with the predicted values from 2009 to 2018 using the ARIMA model. However, the difference between the monitoring and predicted values widened significantly in 2019–2022, ranging from 5.42% in 2019 to 7.56% in 2022 (Table 1).

The analysis of global aggregation indicated that except for 2012, the global Moran's *I* values for the overall detection rates of dental fluorosis in children from 2009 to 2022 were positive. Among these, only in 2009, the statistic was found to be significant ( $Z=1.8811$ ,  $P=0.040$ ), suggesting that the degree of global aggregation followed a random pattern, except for 2009, which showed an aggregated pattern (Table 2).

The local aggregation analysis revealed consistent types of aggregation and geographical distribution across different years. In 2014, a High-high aggregation area was identified in Shanxi, and the northern region consistently showed Low-high aggregation areas in Beijing for six years and in Shandong in 2019. High-low aggregation areas were predominantly located in the southern region, with cases observed in Guangxi for four years and Jiangxi in 2010. The majority of years saw Low-low aggregation areas covering several southern PLADs, including eleven years in Hunan, eight years in Guangdong, seven years in Jiangxi, and two years in both Fujian and Guangxi (Table 2).

After global space-time interaction tests of the

TABLE 1. Monitoring values and ARIMA model predictions of dental fluorosis detection rate in children aged 8–12 years in drinking water fluorosis areas — China, 2009–2022.

Year	Detection rates of dental fluorosis in children (%)		
	Monitoring value	Fitted/predicted value	95% CI
2009	34.87	34.88	–
2010	33.98	34.45	–
2011	32.78	33.22	–
2012	30.81	31.75	–
2013	28.58	29.54	–
2014	27.74	27.29	–
2015	26.55	26.52	–
2016	25.98	25.40	–
2017	22.95	24.80	–
2018	22.07	21.75	–
2019	15.50	20.92	(19.49–22.43)
2020	13.60	19.82	(17.82–22.00)
2021	10.84	18.77	(16.34–21.46)
2022	10.19	17.75	(14.99–20.90)
MAPE	–	2.67	–
$R^2$	–	0.97	–

Abbreviation: ARIMA=autoregressive integrated moving average; MAPE=mean absolute percentage error; CI=confidence interval. "–" indicates no statistic analysis for this year or this index.

detection rate of dental fluorosis among children aged 8–12 years from 2009 to 2022, three clusters were found, including one high-prevalence and two low-prevalence clusters, as shown in Table 3. Among them, the high-prevalence cluster was in Tianjin (LLR=88,828.30,  $P<0.001$ ). The total number of dental fluorosis cases detected in Tianjin from 2017–2022 was more than that of the expected cases, and the *OR* was 2.98. Conversely and apparently, two low-prevalence clusters covered more PLADs, except that in the northeast, and the clustering time was between 2019 and 2022. One low-prevalence cluster was distributed in Henan, Shanxi, and Shandong in 2021–2022 (LLR=21,423.60,  $P<0.001$ ), with the total number of cases of dental fluorosis detected less than the expected one, and the *OR* is 0.58. The other low-prevalence cluster was relatively widely distributed in 11 PLADs, and the *OR* is 0.34 (LLR=40,118.60,  $P<0.001$ ) (Table 3).

## DISCUSSION

This study demonstrates the effective control of dental fluorosis in children residing in areas of China

TABLE 2. Global aggregation analysis and local aggregation areas of dental fluorosis detection rate in children aged 8–12 years in drinking water fluorosis PLADs — China, 2009–2022.

Year	Global aggregation analysis			Localized areas of aggregation			
	Moran's I	Z	P value	High-high agglomeration	High-low agglomeration	Low-high agglomeration	Low-low agglomeration
2009	0.190	1.8811	0.040				Hunan, Jiangxi, Guangdong
2010	0.068	-0.1753	0.465		Jiangxi		
2011	0.008	0.3415	0.344		Guangxi		Hunan, Jiangxi
2012	-0.083	-0.3609	0.377		Guangxi		
2013	0.048	0.6778	0.243			Beijing	Hunan, Jiangxi, Guangdong, Guangxi
2014	0.121	1.2050	0.126	Shanxi			Hunan, Jiangxi, Guangdong, Guangxi
2015	0.052	0.7362	0.234		Guangxi		Hunan, Jiangxi
2016	0.035	0.5698	0.274		Guangxi		Hunan
2017	0.065	0.8128	0.206			Beijing	Hunan, Jiangxi, Guangdong, Guangxi
2018	0.120	1.2333	0.117				Hunan, Jiangxi, Guangdong
2019	0.132	1.5438	0.069			Beijing, Shandong	Hunan, Guangdong
2020	0.084	1.1236	0.147			Beijing	Hunan, Guangdong, Fujian
2021	0.018	0.5549	0.257			Beijing	Hunan, Jiangxi, Guangdong
2022	0.078	1.0321	0.143			Beijing	Hunan, Guangdong, Fujian

Abbreviation: PLADs=provincial-level administrative divisions.

TABLE 3. Global space-time interaction tests for the detection rate of dental fluorosis in children aged 8–12 years in the fluorosis PLADs caused by drinking water fluorosis in China from 2009–2022.

Type of cluster (number)	PLADs	Time (year)	The total number of children detected	The number of fluorosis cases detected	Expected cases	OR	LLR	P value
High-prevalence cluster								
1	Tianjin	2017–2022	554,169	187,221	70,766	2.98	88,828.30	<0.001
Low-prevalence clusters								
11	Yunnan, Guangxi, Chongqing, Sichuan, Hunan, Guangdong, Shaanxi, Gansu, Qinghai, Hubei, Jiangxi	2019–2022	975,218	45,708	124,524	0.34	40,118.60	<0.001
3	Henan, Shanxi, Shandong	2021–2022	1,534,525	122,176	195,940	0.58	21,423.60	<0.001

Abbreviation: OR=odds ratio; LLR=log likelihood ratio; PLADs=provincial-level administrative divisions.

with high levels of fluoride in drinking water. However, variations in the distribution of dental fluorosis exist across different regions and over time. From 2009 to 2022, a significant decrease in the prevalence of dental fluorosis was noted among children aged 8–12 years residing in these areas. In 2014, Shanxi remained in a High-high cluster, while other regions exhibited Low-low, Low-high, or High-low clusters. Although 14 PLADs were identified as

low-probability clusters, Tianjin continued to be classified as a high-probability cluster. The findings of this study have implications for targeted policies, resource allocation, and optimization of prevention and control efforts in relation to the temporal and spatial epidemiological characteristics of drinking water fluorosis.

The analysis of temporal trends indicates a decline in dental fluorosis among children residing in areas with

drinking water fluorosis in China. The observed dental fluorosis detection rates in the period 2019–2022 were significantly lower than the predicted values. The difference between the observed and predicted values increased from 5.42% in 2019 to 7.56% in 2022 with the rate of decrease in an increasing mode, which indicates that the prevention and control of fluorosis in the past five years had significant benefits. This positive outcome can be attributed to the Chinese government's commitment to public health and the implementation of measures outlined in the "Three-year Action Program for the Prevention and Control of Endemic Diseases (2018–2020)". These measures include a focused effort to improve water quality and reduce fluoride content in areas affected by endemic diseases. Consequently, there has been a notable improvement in water quality compliance and a successful control of the risks associated with drinking water fluorosis (4–5).

Spatial analysis revealed that only 2009 exhibited a global aggregation pattern, while all other years displayed a random pattern. Further analysis using LISA identified localized aggregations in different years, primarily concentrated in the southern region of China with low detection rates. This suggests that, apart from the southern region, other regions exhibit a more random distribution, with high detection rates interspersed with low detection rates. The diverse patterns of aggregation across regions may be influenced by the complex geographic environment of China and the varying prevention and control capabilities of each region (6–7).

The results of global space-time interaction tests indicated that the aggregation of dental fluorosis cases was primarily observed in the last five years. Among all the PLADs investigated, only Tianjin exhibited a High-prevalence cluster, while 14 areas showed Low-prevalence clusters. Furthermore, the actual number of children with dental fluorosis in these 14 areas was lower than expected, validating the effectiveness of the three-year endemic disease prevention and control measures (8). Previous studies have highlighted Tianjin as the region most affected by drinking water fluorosis between 2016 and 2020 (9–10). However, our study revealed that the actual number of dental fluorosis cases detected in Tianjin exceeded the expected number, suggesting that the situation in this area remains severe and requires special attention.

This study has several limitations. First, the use of dental fluorosis detection rates in children as a

reflection of the prevalence of fluorosis in a region may underestimate the true extent of the condition due to the wide range of symptoms associated with fluorosis in humans. Second, the clinical examination of dental fluorosis is conducted independently by each province, resulting in inevitable differences and a lack of consistency, despite clear judgment criteria. Lastly, this study primarily focuses on PLADs, which prevents the distinction of key areas within each PLAD. Future research should consider further analysis at the county and even township level to better understand the distribution of fluorosis.

Overall, the prevalence of endemic drinking water fluorosis in China has transitioned from a high regional concentration to a lower overall prevalence. As a result, it is necessary to adjust China's prevention and control policies accordingly. Rather than focusing solely on high-incidence regions, efforts should now be directed towards monitoring and early detection of fluoride exposure, as well as implementing stronger prevention and control measures at the local level. The government should adopt a dynamic approach in optimizing the allocation of resources for fluorosis prevention and control, taking into account changes in the spatial distribution of drinking water fluorosis. Additionally, vigilance should be maintained to prevent the re-emergence of fluorosis hazards in regions with random detection rates. It is crucial to identify the causes behind the aggregation of high-prevalence regions and develop tailored plans to effectively implement prevention and control measures, thus mitigating the risks associated with fluorosis.

**Conflicts of interest:** No conflicts of interest.

**Acknowledgements:** Paula Chacon and Zafar Gazala for their support in methodology, formal analysis, and writing.

**Funding:** Supported by the Committal Project of Health and Immunization Planning Division, National Disease Control and Prevention Administration, 2023; National Natural Science Foundation of China, 82273749; and the Opening Foundation of NHC Key Laboratory of Etiology and Epidemiology, NHCKLEE20230908.

**doi:** 10.46234/ccdcw2024.006

# Corresponding author: Junrui Pei, peijunrui@ems.hrbmu.edu.cn.

<sup>1</sup> Center for Endemic Disease Control, Chinese Center for Disease Control and Prevention; Harbin Medical University, Harbin City, Heilongjiang Province, China; <sup>2</sup> Key Lab of Etiology and Epidemiology, Education Bureau of Heilongjiang Province (23618504), Ministry of Health of PR; Harbin Medical University, Harbin City, Heilongjiang Province, China.

Submitted: November 09, 2023; Accepted: December 18, 2023

## REFERENCES

1. Wei W, Pang SJ, Sun DJ. The pathogenesis of endemic fluorosis: research progress in the last 5 years. *J Cell Mol Med* 2019;23(4):2333 – 42. <http://dx.doi.org/10.1111/jcmm.14185>.
2. Li Z, Que WJ, Wang T, Ma YZ, Meng XY, Sowanou A, et al. Current status of global endemic fluorosis and measures for its prevention and control. In: *Proceedings of the Eleventh National Conference on Endemic Diseases*. China, 2023. *Chinese Journal of Endemiology*. 2023;42:11. (In Chinese)
3. Center for Endemic Disease Control, Chinese Center for Disease Control and Prevention. The 2020 report of national drinking water endemic fluorosis monitoring: Center for Endemic Disease Control, Chinese Center for Disease Control and Prevention. 2021. [2023-11-23]. <https://www.hrbmu.edu.cn/dbzx/fzjc/dfxfzd.htm>. (In Chinese)
4. Gao YH. Interpretation of the tasks of the special three-year program for prevention and control of endemic diseases (2018-2020). *Chin J Endemiol* 2019;38(1):1 – 3. <http://dx.doi.org/10.3760/Cma.J.Issn.2095-4255.2019.01.001>. (In Chinese).
5. Liu H, Gao YH, Shen HM, Sun DJ. Achievement during the 13th Five-Year Plan and analysis of the 14th Five-Year Plan on prevention and control of endemic diseases in China. *Chin J Endemiol* 2022;41(3): 176 – 9. <http://dx.doi.org/10.3760/Cma.J.Cn231583-20220302-00056>. (In Chinese).
6. Liu H, Gao YH. The progress, important experience and ideas for the next step of three-year special program for control of endemic diseases in China. *Chin J Endemiol* 2020;39(1):1 – 3. <http://dx.doi.org/10.3760/cma.j.issn.2095-4255.2020.01.001>. (In Chinese).
7. Chang CY. Introduction to the division and characterization of hydrogeological types of coal mines in China. *West-China Exploration Eng* 2021;33(11):132 – 3. <http://dx.doi.org/10.3969/j.issn.1004-5716.2021.11.044>. (In Chinese).
8. Gao YH. Endemic disease control effective in helping people in disease areas running for prosperity. *China Med News* 2021;36(1):12. <http://dx.doi.org/10.3760/cma.j.issn.1000-8039.2021.01.111>. (In Chinese).
9. Zhang L, Zhao L, Zeng Q, Fu G, Feng BJ, Lin XH, et al. Spatial distribution of fluoride in drinking water and health risk assessment of children in typical fluorosis areas in North China. *Chemosphere* 2020;239:124811. <http://dx.doi.org/10.1016/j.chemosphere.2019.124811>.
10. Fan SL. Current prevention and control of endemic fluorosis during the Thirteenth Five-Year Plan in China. *J Environ Occup Med* 2020;37(12):1219 – 23. <http://dx.doi.org/10.13213/j.cnki.jeom.2020.20274>. (In Chinese).