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Assessing the influencing factors of dengue fever in Chinese mainland based on causal analysis

Xingyuan Yu¹, Xia Wang¹✉ & Sanyi Tang²

Previous studies have identified various factors affecting dengue fever, but most focus on correlations within specific regions, not establishing causality. This study uses Convergent Cross Mapping (CCM) to explore the causal relationships between nine meteorological factors and reported dengue fever cases in 14 Chinese provinces with the highest incidence. Results show that temperature and pressure have causal links with case numbers in more provinces. In Guangdong, which has the most reported cases, Partial Cross Mapping (PCM) reveals a direct causal relationship only between GDP and reported dengue fever cases, while meteorological factors influence dengue fever via their impact on mosquito populations. Principal Component Analysis (PCA) from 30 provinces further confirms the importance of temperature and pressure. Given the significant negative correlation between temperature and pressure, separate models were developed for each province using the Distributed Lag Nonlinear Model (DLNM) combined with the Generalized Additive Model (GAM), with GDP as a covariate. The results indicate that the Relative Risk (RR) increases significantly under high temperatures and low pressure within a shorter lag period. GDP significantly promotes case numbers in all provinces.

Keywords Dengue, Convergent cross mapping, Partial cross mapping, Generalized additive model, Lag, Distributed lag nonlinear model

Dengue fever is one of the most concerning public health issues worldwide. It is predicted that 2.25 (1.27–2.80) billion more people will be at risk of dengue in 2080 compared to 2015, totaling 6.1 (4.7–6.9) billion, or over 60% of the world's population¹. Dengue is endemic in more than 100 countries across tropical and subtropical regions worldwide². The cases that are reported are 100 million of dengue fever each year, and up to 500,000 go on to develop the infection's potentially fatal dengue hemorrhagic fever or dengue shock syndrome³. The first reported outbreak of dengue fever in China occurred in 1978 in Guangdong Province, Southeast China⁴. Since then, cases of dengue fever have been reported in China every year⁵, with the disease gradually spreading from the Southeast coastal region to central and Western China⁶.

Dengue virus and its vector, the Aedes mosquito, are known to be sensitive to climate conditions⁷. Climate change may increase the suitability of dengue transmission in temperate regions and expand the global population at risk of these diseases⁸. Temperature is one of the most commonly studied variables affecting dengue⁹. Both the virus's extrinsic incubation period and various physiological characteristics of the mosquito (such as reproduction, development, survival, and biting rate) are related to temperature^{10–14}. Temperature affects virus transmission by mosquitoes¹⁵. Transmission occurs between 18 and 34 °C, with maximal transmission occurring in the range of 26–29 °C¹⁶. In addition to studying the impact of temperature on Aedes mosquitoes, some research has directly examined the effect of temperature on the number of dengue cases^{17,18}. This includes mean temperature, minimum temperature, and maximum temperature, all of which have nonlinear impacts on dengue¹⁹. Some studies have also discussed the Indian Ocean Basin-wide index, which reflects the consistent sea temperature changes in the tropical Indian Ocean region. These changes can influence the prevalence of dengue fever by altering local temperatures²⁰.

Research indicates that factors such as relative humidity, rainfall, and wind speed are all associated with the outbreak of dengue fever^{21,22}, and their impacts vary²³. A study by Caldwell et al. indicates that humidity is positively associated with mosquito survival because the high surface area to volume ratio of mosquitoes exposes them to desiccation¹¹. Standing water from rainfall provides essential larval and pupal habitats for mosquitoes, but the relationship is complex because heavy rainfall can flush away breeding habitats^{24–26}. Water-storage practices during a drought can increase water availability, mosquito abundance, and contact between

¹School of Mathematics and Statistics, Shaanxi Normal University, Xi'an 710119, People's Republic of China.

²School of Mathematical Sciences, Shanxi University, Taiyuan 030006, People's Republic of China. ✉email: xiawang@snnu.edu.cn

mosquitoes and people^{27–29}. Additionally, the impact of meteorological factors shows regional variations in lag²⁷. These meteorological factors not only affect mosquitoes differently but also exhibit significant regional variations in their impact on case numbers. For instance, studies indicate that in Bangladesh, rainfall has a significantly positive impact on the transmission of dengue fever³⁰. However, in Bangkok, the amount of rainfall (lagged by three months) is negatively correlated with the incidence of dengue fever³¹. Wind speed and atmospheric pressure also affect the number of cases differently in various regions. Research in Malaysia, Paraguay, and Bangladesh all show that dengue fever cases are negatively correlated with wind speed^{32–34}. However another study on Peru concludes that average wind speed is positively correlated with the monthly incidence rate of dengue fever³⁵. Furthermore, the prevalence of dengue fever is also related to atmospheric pressure³⁶. A study by Chen and colleagues in Guangzhou found a statistically significant negative correlation between atmospheric pressure and the number of dengue fever cases³⁷, while a study in Paraguay suggests a positive correlation between atmospheric pressure and dengue fever³².

The prevalence of dengue fever is influenced not only by meteorological factors but also by population and economic factors. The impact of population density can be quantified through mechanistic models, such as the basic reproduction number¹⁶. However, other economic factors, such as gross domestic product (GDP), are harder to quantify. Kache et al. developed an “urban systems framework” to understand Aedes-borne diseases, exploring how individuals and social structures interact with the biophysical environment. This framework advances considerations for implementing interventions, including urban planning (for example, piped water provisioning) and emerging vector control strategies (for example, Wolbachia-infected mosquitoes) to prevent and control the growing threat of Aedes-borne diseases³⁸. A study conducted in 2022 analyzed the temporal trends of dengue fever incidence at global and regional levels and predicted the incidence rates of dengue fever in 204 countries and regions from 1990 to 2019³⁹. The results indicate that policymakers should pay particular attention to the negative impact of urbanization on dengue fever incidence and allocate more resources to areas with low Sociodemographic Index to alleviate the burden of dengue fever. A study conducted in 2024 found that per capita GDP can amplify the impact of earlier epidemics on the spread of later epidemics, while population density may increase the risk of local dengue fever outbreaks⁴⁰. A study on the relationship between dengue fever, climate, and tourists in Padang found that the number of monthly dengue fever cases was positively correlated with average temperature, precipitation, humidity, and the number of local tourists, but negatively correlated with the number of foreign tourists⁴¹.

In summary, previous studies have shown numerous factors affecting dengue fever. However, related research mainly focuses on correlation analysis of single regions and a limited number of factors. Nevertheless, correlation does not imply causation. Additionally, past research indicates that the impact of meteorological factors on dengue fever outbreaks varies significantly by region⁴². Most studies on the factors influencing dengue fever in China have focused on Guangdong Province. However, with the warming climate, the habitat range of the dengue fever vector, Aedes mosquitoes, continues to expand. This implies that future dengue fever risk areas and populations at risk in China will continue to increase⁴³. China's vast territory results in significant differences in population, economy, and climate across regions. China has a rich diversity of climate types. The southern regions are mainly characterized by subtropical and tropical monsoon climates, with warm temperatures and abundant precipitation throughout the year, particularly during the summer when rainfall is plentiful. The northwestern regions, on the other hand, are predominantly characterized by a temperate continental climate, which is dry and rain-scarce with a large annual temperature range^{44,45}. Dengue case reports are primarily concentrated in southern China, typically peaking in September. The annual amplitude of dengue outbreaks varies with latitude, with larger amplitudes in southern cities and smaller amplitudes in northern cities⁴⁶. Given these specific circumstances, it is both highly relevant and challenging to comprehensively examine the causal relationships between these factors and the number of dengue fever cases (mosquito-borne). This involves exploring the key influencing factors within individual regions and systematically analyzing the regional characteristics and patterns of how the same factor affects different areas.

To address the aforementioned issues, this study employs the Convergent Cross Mapping (CCM) method to investigate the causal relationships between nine meteorological factors and dengue fever cases in the 14 provinces with the highest number of cases in China, considering the climatic characteristics and population economic features of each region. Furthermore, in Guangdong Province, which has the highest number of cases, the Partial Cross Mapping (PCM) method is used to distinguish between the direct and indirect causal relationships among mosquito numbers, dengue fever cases, and influencing factors. Lastly, by constructing regression models for each province, we explore the time-lagged impact and nonlinear effects of key influencing factors in various regions. This reveals regional differences and general patterns, which not only helps to understand the specific mechanisms of various variables in each province but also provides a scientific basis for formulating more targeted public health policies.

Results

The causal relationship between factors and reported cases

In this study, we collected data from 30 provinces across mainland China. However, CCM revealed that in regions with cumulative case numbers not exceeding 200, causal relationships were not significant, and the results were unreliable. Therefore, these regions were excluded from the CCM. We selected regions with cumulative case numbers exceeding 200, totaling 14 provincial administrative areas for discussion. The data for these regions includes monthly case numbers and nine meteorological indicators from February 2005 to December 2019 (see supplementary Fig.S1–Fig.S14). In addition, the dengue fever reported cases in Guangdong Province from 2016 to 2019, mosquito surveillance data, and corresponding meteorological indicators were incorporated into the PCM. For detailed information on the data sources and descriptions, please refer to the Methods section.

CCM analysis results indicate that, at a significance level of 0.05, there is no significant causal influence of meteorological factors on the number of reported cases in all provinces. The P-values of the tests for each meteorological factor and the number of reported cases are shown in Table S1-S2 in the supplementary. To comprehensively analyze the causal relationship between nine meteorological factors and the number of reported cases in 14 provinces, we have summarized the causal analysis results for the 14 provinces (Fig. 1). According to the CCM results, both average temperature(T) and minimum temperature(Tn) exhibit a significant causal relationship with the number of reported cases in eight provinces. Meanwhile, maximum temperature(Tx), dew point temperature(Td), and atmospheric pressure(P) show significant causal effects on the number of reported cases in seven provinces. However, the impact range of horizontal visibility(VV), precipitation(RRR), relative humidity(U), and wind speed(Ff) is relatively small, showing significant causal relationships only in Sichuan, Guangdong, Fujian, Zhejiang, and Yunnan provinces. It is noteworthy that these provinces are affected not only by visibility, precipitation, humidity, and wind speed but also by temperature and atmospheric pressure.

For example, in Zhejiang Province, the CCM final values for the four temperature variables are all greater than 0.6, with atmospheric pressure at 0.52, and visibility being the lowest at 0.42. The data from Fujian Province shows a similar pattern, with the final values for the four temperature variables all above 0.7, atmospheric pressure at 0.66, and visibility and rainfall at 0.6 and 0.41, respectively. This indicates that temperature and atmospheric pressure not only affect more provinces but also have a significantly higher impact within the same province compared to factors like visibility.

Figure 2 specifically displays the CCM results for Guangdong Province, which has the highest number of reported cases. Results for other provinces are shown in the supplementary Fig.S15-Fig.S27. According to Fig. 2, the minimum temperature, maximum temperature, average temperature, dew point temperature, atmospheric pressure, horizontal visibility, and rainfall, all have a significant impact on the number of reported cases in Guangdong Province, with all these factors having a P-value of 0, indicating a clear causal relationship.

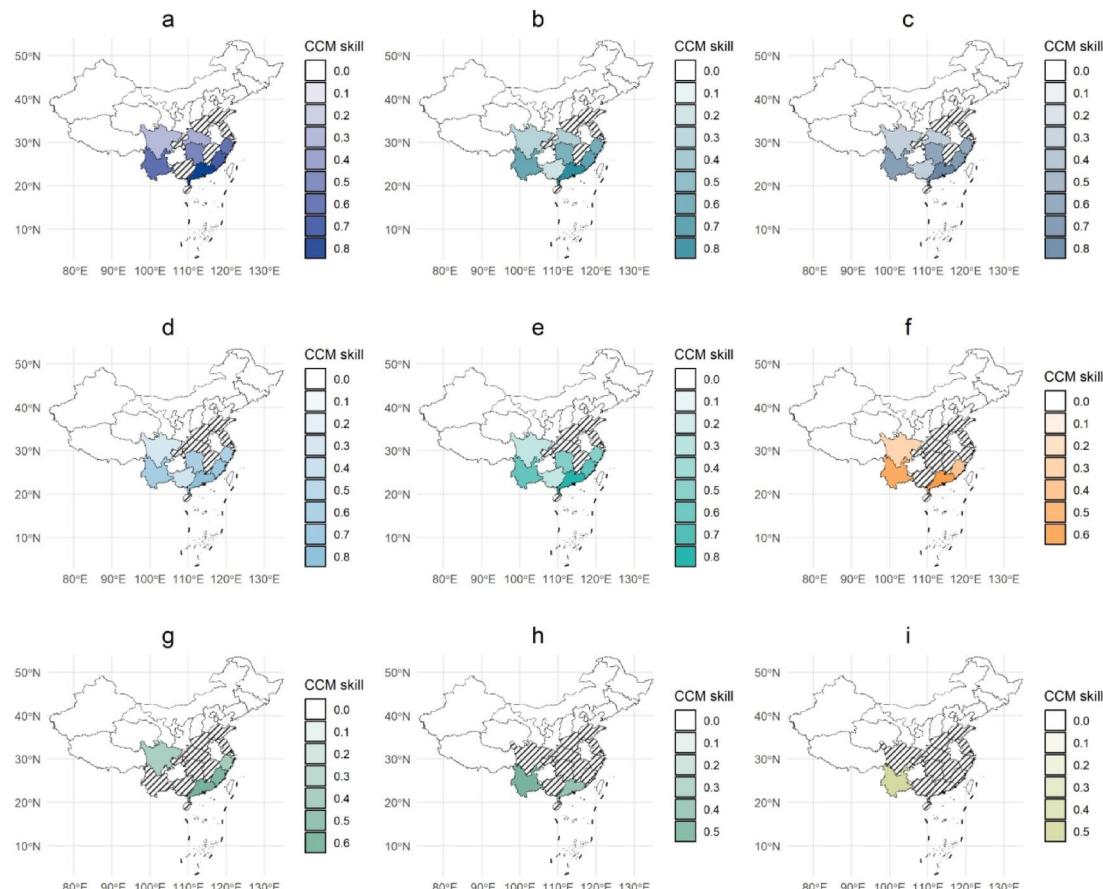


Fig. 1. Causal analysis results of the 14 provinces with the highest number of reported cases and nine meteorological factors($P \leq 0.05$). In the nine subplots, each map displays the CCM skill between a specific meteorological factor and the number of reported cases in each province: (a)Tx. (b)T. (c)Tn. (d)Td. (e)P. (f)RRR. (g)VV. (h)U. (i)Ff. On these maps, varying shades of color represent the final value size of the CCM analysis results, with darker colors indicating a stronger causal relationship between the meteorological factor and the number of reported cases. For regions where a specific meteorological factor has no significant causal relationship with the number of reported cases, grey diagonal stripes are used for differentiation. Additionally, white areas on the map indicate regions not included in this study.

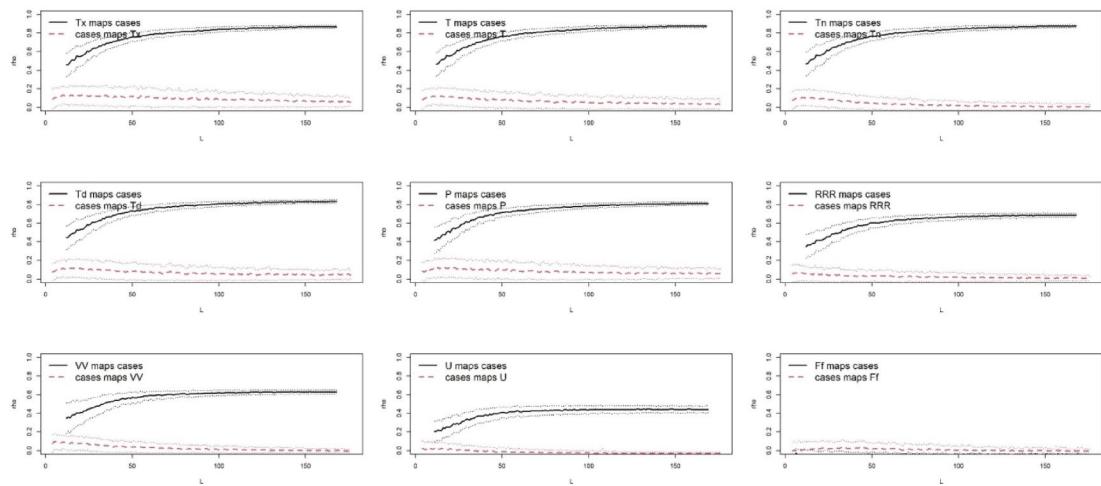


Fig. 2. Causal analysis results between nine meteorological factors and the number of reported cases in Guangdong Province. Each subplot shows the variation of the CCM skill between a specific meteorological factor and the number of reported cases as the time series increases. With dashed lines on both sides representing the standard error (confidence interval) of the CCM skills.

	GDP	Tx	T	Tn	Td	P	RRR	VV	U	Ff
PCM on factors causes cases	0.413	0.269	0.172	0.171	0.103	0.172	0.118	0.131	0.150	0.030
p-values	0.000	0.001	0.029	0.030	0.195	0.030	0.135	0.096	0.058	0.706

Table 1. PCM results between factors and reported dengue fever cases in Guangdong Province.

Additionally, the P-value for humidity is 0.035, which, under the set significance level of 0.05, indicates a significant impact of humidity on the number of reported cases in Guangdong Province. In contrast, the P-value for wind speed is 0.875, indicating that wind speed does not have a significant impact on the number of reported cases in Guangdong Province. On the other hand, given a significance level of 0.05, the number of reported cases in Guangdong Province does not significantly affect all meteorological factors, which is consistent with the actual situation.

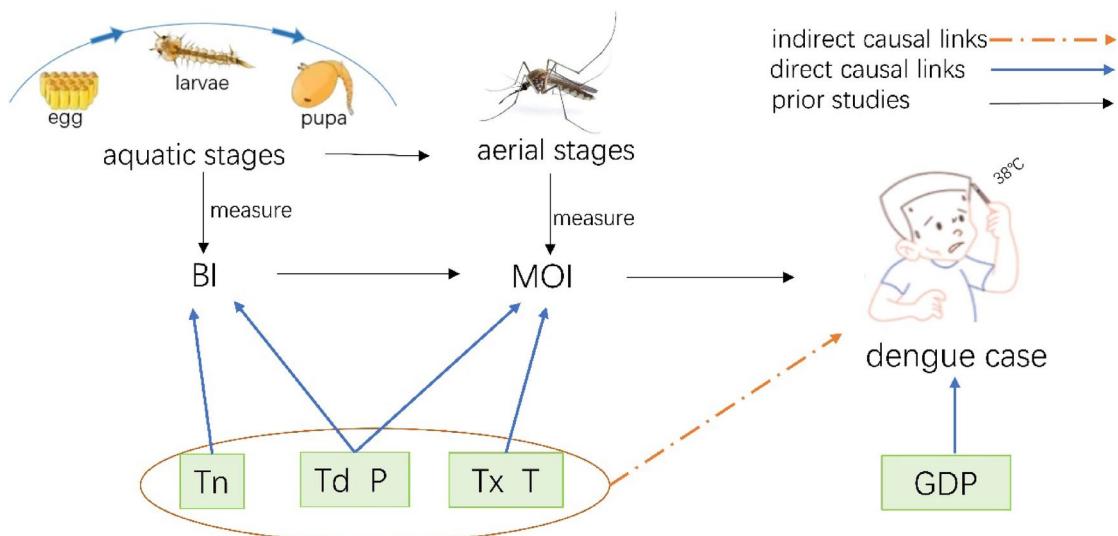
Additionally, with the increase of the time series, the CCM skill gradually increases and eventually stabilizes at a high final value. The lowest CCM skill is for the impact of humidity on the number of reported cases, with a value of approximately 0.44, followed by visibility and rainfall, with values of 0.63 and 0.68, respectively. The final CCM skill values for the four temperature variables and atmospheric pressure, with respect to the number of reported cases, all exceed 0.8. This indicates that using CCM analysis to study the causal relationship between various meteorological factors and the number of reported cases in Guangdong Province is effective, and each identified meteorological factor has a significant impact on the number of reported cases.

Considering the potential transitivity in CCM results, the PCM method was used to distinguish the direct and indirect causal relationships between meteorological factors and the number of reported cases. PCM and CCM were conducted separately. Since only mosquito-borne data for Guangdong Province were available, PCM analysis was performed only for Guangdong. The PCM results show that under the given threshold of 0.4⁴⁷ and a significance level of 0.05, none of the meteorological factors have a significant direct causal relationship with the number of reported cases in Guangdong Province. Considering that the original GDP data is more abundant than the population data, the PCM was further performed between Guangdong Province's GDP and the number of reported cases. The results in Table 1 indicate that GDP has a significant direct causal relationship with the number of reported cases, while the number of reported cases does not have a significant direct causal effect on any of the factors.

The results indicate that weather conditions do not directly affect the number of reported dengue fever cases. However, dengue fever is a mosquito-borne infectious disease, so further PCM analysis was conducted on weather factors with mosquito ovitrap index(MOI) and Breteau index (BI) to investigate whether weather factors indirectly affect the number of reported dengue fever cases by directly influencing mosquito populations. MOI and BI have no significant direct causal relationship with all meteorological factors. The results in Table 2 show that maximum temperature, average temperature, dew point temperature, and atmospheric pressure have a significant direct causal relationship with MOI, while minimum temperature, dew point temperature, and atmospheric pressure have a significant direct causal relationship with BI.

Based on the aforementioned research findings, a causal relationship diagram is illustrated in Fig. 3. Previous studies have demonstrated that the number of mosquitoes in the aquatic stages (measured as BI) affects the number of mosquitoes in the aerial stages (measured as MOI), The number of mosquitoes in the aerial stages

	Tx	T	Tn	Td	P	RRR	VV	U	Ff
PCM on factors causes MOI	0.484	0.402	0.316	0.497	0.553	0.204	0.221	0.061	0.138
p-values	0.005	0.023	0.078	0.004	0.001	0.263	0.224	0.741	0.452
PCM on factors causes BI	0.264	0.356	0.464	0.486	0.516	0.214	0.070	0.343	0.222
p-values	0.144	0.046	0.007	0.005	0.003	0.239	0.705	0.055	0.223

Table 2. PCM results between factors and MOI and BI in Guangdong Province.**Fig. 3.** The causal relationship between factors within Guangdong Province and the number of reported dengue fever cases.

may potentially spread dengue fever within populations. Indirect methods for measuring mosquitoes can effectively reflect the actual changes in case numbers in most situations^{48–52}. PCM analysis results indicate a direct causal relationship between GDP and the number of reported dengue fever cases. Additionally, maximum temperature, average temperature, minimum temperature, dew point temperature, and atmospheric pressure have a direct causal relationship with the number of mosquitoes. Therefore, maximum temperature, average temperature, minimum temperature, dew point temperature, and atmospheric pressure indirectly influence the number of reported dengue fever cases by affecting the mosquito population.

Selection of important and representative factors

To verify the results of comparative causal analysis and select the most important and representative variables from meteorological factors, GDP, and population, we conducted PCA on the collected data for 30 provinces. The results of PCA indicate that the selection of the first four principal components achieves over 90% cumulative contribution rates in all regions except Anhui Province. Therefore, the first four principal components were chosen for further analysis, and the original variables with high absolute values in these principal components were studied in greater detail.

As shown in Fig. 4, in the first principal component, the factor loadings of temperature variables have the highest absolute values across all provinces. Except for Yunnan and Qinghai, in the first principal component of all other provinces, the factor loading of pressure follows closely behind temperature in terms of absolute value. In Qinghai Province, the sequence of factor loading absolute values in the first principal component is temperature, humidity, and then pressure; whereas in Yunnan Province, the pressure has the largest factor loading in the second principal component. These findings validate the importance of temperature and pressure indicated in the causal analysis results. Furthermore, the PCA reveals that the types of temperature variables with the highest factor loadings vary across different provinces. In 80% of the provinces, either population or GDP exhibits the largest factor loading absolute value in the second principal component. For the third and fourth principal components, humidity and wind speed tend to have the highest factor loading absolute values in more provinces.

Regression analysis

In the aforementioned analysis, factors found to have a causal relationship with the number of reported cases in most provinces are temperature and pressure. Furthermore, temperature, pressure, and GDP have larger factor loadings in absolute values in the principal component analysis results of most provinces. In this section, regression models were established for each province to explore the impact of temperature, pressure, and GDP

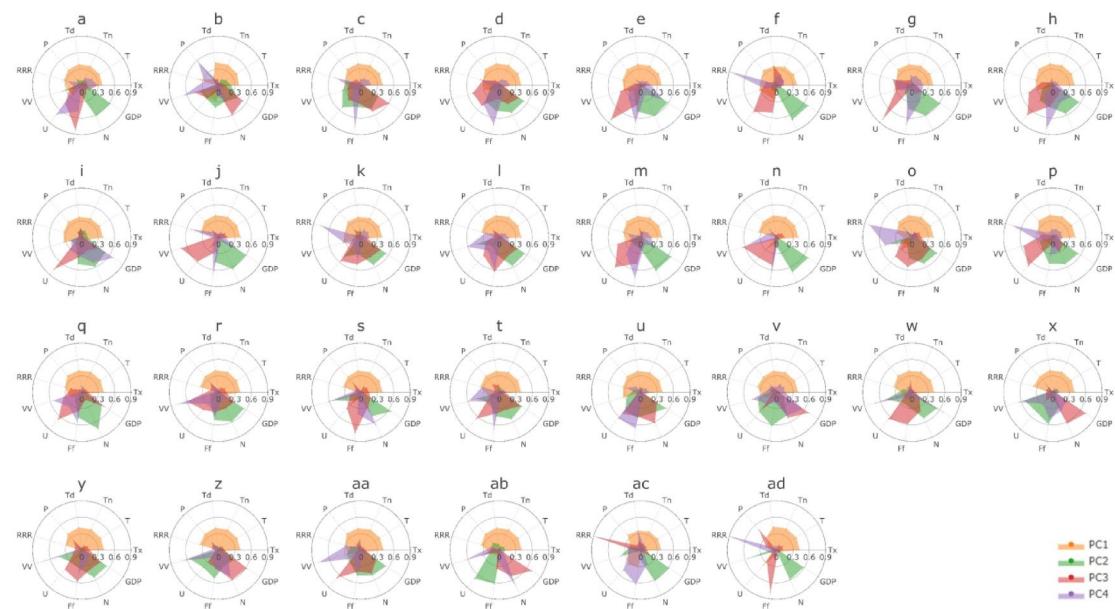


Fig. 4. Visualization of the top four principal components by the absolute value of factor loadings in 30 provinces: (a) Guangdong, (b) Yunnan, (c) Fujian, (d) Zhejiang, (e) Guangxi, (f) Chongqing, (g) Jiangxi, (h) Hunan, (i) Sichuan, (j) Henan, (k) Hainan, (l) Jiangsu, (m) Hubei, (n) Shandong, (o) Beijing, (p) Shanghai, (q) Anhui, (r) Hebei, (s) Liaoning, (t) Shaanxi, (u) Guizhou, (v) Heilongjiang, (w) Gansu, (x) Jilin, (y) Tianjin, (z) Shanxi, (aa) Ningxia, (ab) Inner Mongolia, (ac) Xinjiang, and (ad) Qinghai.

on reported dengue fever cases. Given their significant causal influence and strong statistical correlation (see supplementary Fig.S28–Fig.S41), temperature and pressure were analyzed separately. Generalized Additive Models (GAM) were used to account for potential nonlinear effects^{16,53}, with GDP as a covariate. Meteorological factors can have a lagged effect on dengue fever^{11,27,54}. To account for this lagged effect, we used a distributed lag non-linear model (DLNM) to model the non-linear relationship and lagged effects of meteorological factors (such as temperature or pressure). Model summary in Table S3–S4 in the supplementary. Analysis was conducted only for 14 provinces with over 200 cumulative reported cases to avoid confounding factors. Temperature variables were selected based on principal component analysis, prioritizing those with higher loadings and established causal relationships.

As shown in Fig. 5, for all provinces, within a shorter lag period, the relative risk (RR) significantly increases and reaches a peak as temperatures rise. In contrast, at lower temperatures and longer lag times, the RR is relatively low. Furthermore, we have observed that under the longest lag time conditions, as temperatures decrease, the RR shows abnormally high peaks in some provinces.

As shown in Fig. 6, the regression results indicate that for all provinces, within a shorter lag period, the RR value increases as the pressure decreases, until a peak is reached. Additionally, under extreme conditions, such as the highest or lowest pressure levels, and with the longest lag times, the RR in some provinces may exhibit abnormally high values. The dynamic changes in the lag effect also demonstrate that within a shorter lag period, the RR value increases significantly, but its impact gradually diminishes as the lag time extends.

In the regression models for temperature and pressure, both consider GDP as a covariate and use spline smoothing functions for fitting. The results show that the differences in the impact of GDP on case numbers across provinces are minimal in both models. Figure 7 presents the effect of GDP on case numbers in the temperature model, while the impact of GDP in the pressure model can be found in the supplementary Fig.S42. The results from all provinces consistently indicate that as GDP increases, there is an overall upward trend in its impact on case numbers.

Discussion

Our model is only effective for regions with a cumulative number of reported cases greater than 200. Because in conducting causal analysis, we need a longer time series to ensure the effectiveness and accuracy of the model. When the cumulative number of reported cases is less than 200, the time series may contain a large number of zeros, which can interfere with the final results. The CCM results for the 14 provinces with a cumulative number of reported cases greater than 200 indicate that temperature and pressure have a significant causal relationship with the number of reported dengue fever cases in most provinces, suggesting a widespread causal effect of temperature and pressure on the number of reported cases (Fig. 1). When comparing the CCM final values of different factors affecting the number of reported cases within a single province, it is found that the CCM final values for temperature and pressure are higher than those for other factors, suggesting that temperature and pressure have a stronger causal influence on the number of reported cases compared to other factors (Fig. 2). When comparing the number of reported cases and the number of meteorological factors with a causal

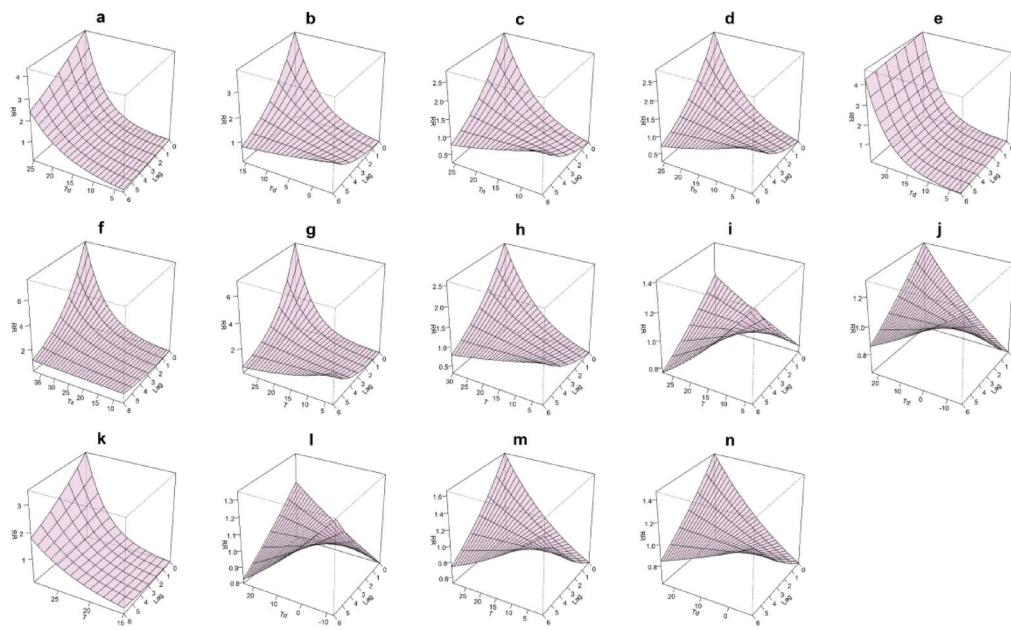


Fig. 5. Three-dimensional plot of the relationship between temperature and reported cases RR over 6 lag months. (a)Guangdong, (b)Yunnan, (c)Fujian, (d)Zhejiang, (e)Guangxi, (f)Chongqing, (g)Jiangxi, (h)Hunan, (i)Sichuan, (j)Henan, (k)Hainan, (l)Jiangsu, (m)Hubei, and (n)Shandong.

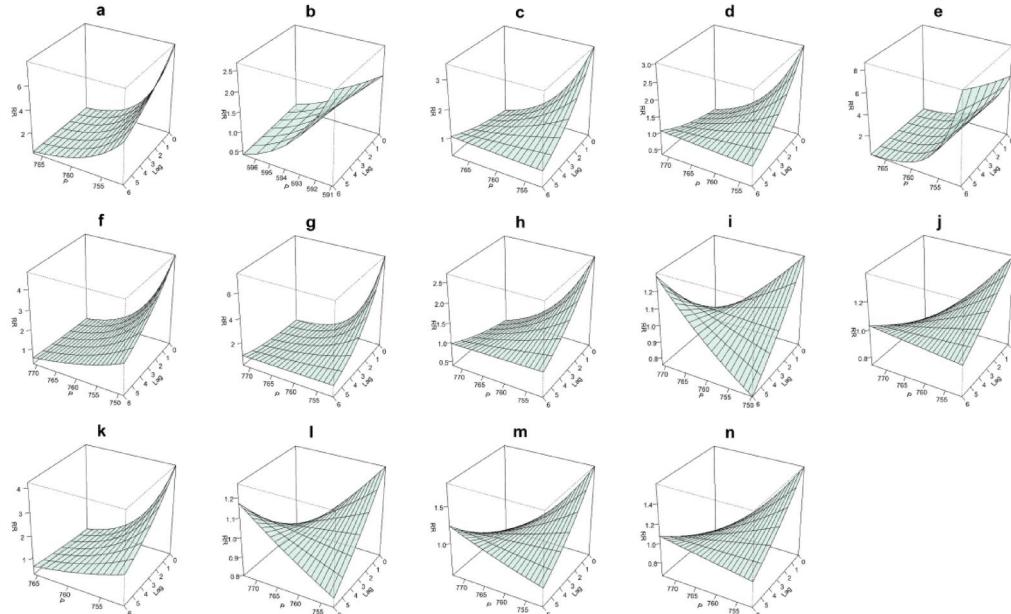


Fig. 6. Three-dimensional plot of the relationship between pressure and reported cases RR over 6 lag months. (a)Guangdong, (b)Yunnan, (c)Fujian, (d)Zhejiang, (e)Guangxi, (f)Chongqing, (g)Jiangxi, (h)Hunan, (i)Sichuan, (j)Henan, (k)Hainan, (l)Jiangsu, (m)Hubei, and (n)Shandong.

relationship in all provinces, it is observed that areas with more reported cases are also influenced by a greater number of meteorological factors (Fig. 1). This may be because in areas with fewer reported cases, a significant portion of the reported cases are imported from other regions, making them more influenced by factors such as population movement. In areas with more reported cases, local transmission accounts for the majority, which allows for a better demonstration of the role of meteorological factors.

The PCM results from Guangdong Province indicate that temperature and pressure have a significant direct causal relationship with the number of mosquitoes but do not directly affect the number of dengue fever reported cases (Fig. 3). This supports the view that meteorological factors indirectly influence the spread of

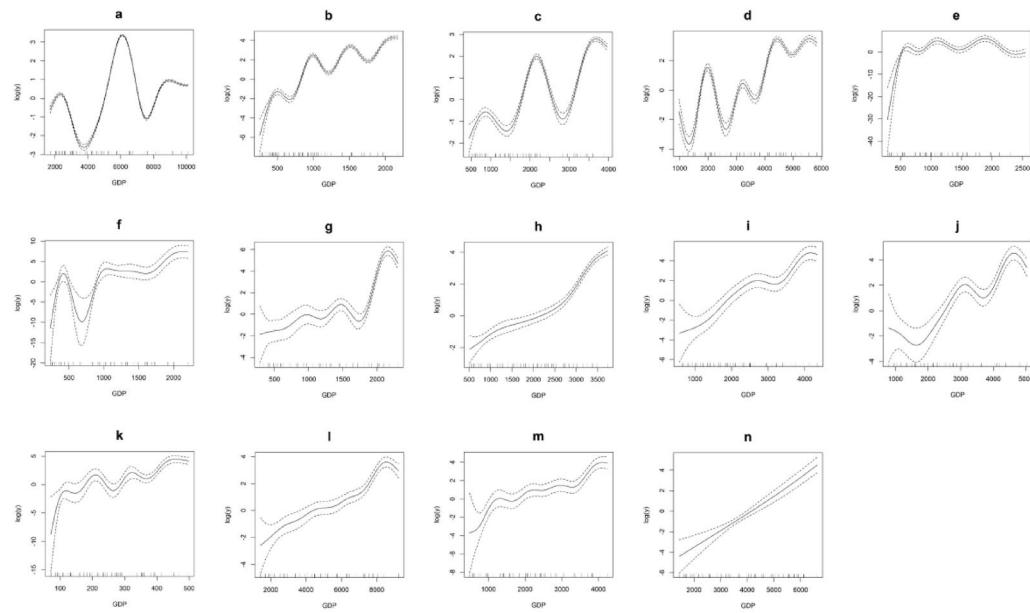


Fig. 7. Smooth effects of provincial GDP on the logarithm of case numbers in the DLNM-GAM temperature model: (a)Guangdong, (b)Yunnan, (c)Fujian, (d)Zhejiang, (e)Guangxi, (f)Chongqing, (g)Jiangxi, (h)Hunan, (i)Sichuan, (j)Henan, (k)Hainan, (l)Jiangsu, (m)Hubei, and (n)Shandong.

dengue fever by affecting the mosquito population. The PCM results suggest that the minimum temperature only affects mosquito larvae, while the maximum temperature only affects adult mosquitoes. Previous studies have also mentioned that at lower temperatures, larvae remain motionless and die within a few days⁵⁵, while the survival rate of adult mosquitoes significantly decreases at higher ambient temperatures⁵⁶. This may be because larvae live in water bodies with a lower metabolic rate and are highly sensitive to temperature changes. The minimum temperature affects the development speed, growth cycle, and survival rate of larvae. Adults are terrestrial insects, and excessively high temperatures can lead to excessive evaporation and water loss, affecting their survival and reproductive capabilities. Extremely high temperatures (above 40 °C) can cause heat stress, and even death, making adults sensitive to maximum temperatures.

Further principal component analysis across the 30 provinces revealed results consistent with the causal analysis. In the first principal component, temperature and pressure once again had the highest loadings (Fig. 4), which fully demonstrates the significant impact of temperature and pressure on the spread of dengue fever. Correlation analysis results indicate that in the 14 provinces we focused on, temperature and pressure exhibit a strong negative correlation, with the correlation coefficient exceeding 90% in 13 provinces. In the correlation analysis, only Yunnan province had a temperature-pressure correlation coefficient below 0.9. Yunnan has the highest altitude and the lowest average pressure during the study period. Its unique geographical location is likely one of the reasons why the correlation coefficient between temperature and pressure was around 0.5 in Yunnan.

The results of the regression analysis indicate that the effects of temperature and pressure on disease transmission exhibit certain similarities in their overall trends. Specifically, in environments with higher temperatures (or lower pressure), the RR shows a gradual upward trend, suggesting that high temperatures (or low pressure) may promote an increase in the number of reported cases. Conversely, when temperature is lower (or pressure is higher), the RR is significantly below 1, indicating that low temperatures (or high pressure) may reduce the risk of disease transmission. Further analysis reveals that the impact of temperature and pressure on disease transmission exhibits nonlinear characteristics, with warm and low-pressure environments potentially providing more favorable conditions for pathogen spread. This phenomenon is particularly pronounced over shorter time lags, suggesting that current meteorological conditions have a direct and strong influence on case numbers. However, as the time lag increases, the effect of meteorological factors on disease transmission risk gradually diminishes, indicating that their influence is time-sensitive.

Under extreme conditions, such as the lowest temperatures or the highest/lowest pressures with the longest lag times, the RR may exhibit abnormally high values. This phenomenon could be due to the delayed impact of extreme temperatures or pressures from several months prior on the incidence rate, or it could be a result of estimation bias caused by a smaller sample size, both of which require further research and validation. The DLNM can capture complex non-linear and interaction effects through high-dimensional structures. However, this flexibility may also lead to overfitting in extreme data points, such as those with extremely low temperatures or long lag periods. In particular, when there are few observations of extremely low temperatures, the model may amplify minor variations, resulting in abnormally high predicted values. Whether it is temperature or pressure, these abnormally high-value points correspond to very few data points. Taking Sichuan Province as an example, when the T is below 5 °C, no cases are reported, and only 44 cases are reported when it is below 10 °C (a total

of 526 cases). When the pressure is above 770 mmHg, no cases are reported, and 74 cases are reported between 765 and 770 mmHg.

In the PCM analysis of Guangdong Province, the results indicate that there is a significant direct causal relationship only between GDP and the number of reported dengue fever cases. This highlights the importance of GDP. The regression results show that as GDP increases, it has a promoting effect on the number of reported cases in all provinces, but the specific impact varies by province. The fluctuations in the curves may be related to different conditions in each province at different times, including major outbreaks in a particular year⁵⁷ and artificial fluctuations in GDP, etc.

The complex relationship between levels of economic activity and disease transmission has been revealed. While high levels of economic activity can lead to better public health resources, they also increase opportunities for crowd gatherings and mobility, thereby facilitating the spread of infectious diseases. Economically developed areas face greater challenges in epidemic prevention and control, and therefore need to adopt stricter and more scientific measures to effectively control the spread of the epidemic.

This study takes into account the specific national conditions of China, comprehensively considering meteorology, population, society, and regional differences. It systematically reviews the factors affecting dengue fever in various provinces of China. Using the CCM method and principal component analysis, the study explores the key influencing factors in a single region, highlighting the significant impact of temperature and pressure. The PCM results further indicate that GDP directly affects the number of reported dengue fever cases, while temperature and pressure influence the number of mosquito populations, which in turn indirectly affect dengue fever. Considering the strong negative correlation between temperature and pressure, regression models are separately established, providing specific patterns and lag effects of temperature and pressure on case numbers in different provinces. The study results reveal the important influence of temperature, pressure, and GDP on the number of reported dengue fever cases and their regional characteristics. An in-depth analysis of these key variables can provide scientific evidence for formulating prevention and control strategies.

This study also has some limitations. First, the CCM method does not apply to regions with a small number of reported cases, so these areas were excluded from the study, which limits the comprehensiveness of the results. Second, when using PCM to analyze the relationship between GDP and the number of reported cases in Guangdong Province, the GDP data were obtained by averaging the original data. Lastly, due to the cumulative reported cases accounting for only 6.6 per 100,000 of the total population and the lack of corresponding serotype data, the study did not consider changes in population susceptibility or serotype circulation, which may introduce certain limitations to the research findings. We will further investigate these issues in subsequent studies.

Methods

Data on cities and reported dengue fever cases

This paper collects the monthly reported dengue fever cases in provinces of China from February 2005 to December 2019 for study within this range. The data is sourced from The Data-center of China Public Health Science(<https://www.phsciencedata.cn/Share/>), managed by the Chinese Center for Disease Control and Prevention. The study involves 93,699 reported dengue fever cases, covering 30 provincial-level administrative regions in mainland China (data from the Tibet Autonomous Region was excluded due to high missing rates). Among these, eight provinces had accumulated over 1,000 reported cases, with Guangdong Province having the highest number at 63,510 reported cases, followed by Yunnan Province with 13,917 reported cases. Additionally, 14 provinces had accumulated more than 200 reported cases, including Guangdong, Yunnan, Fujian, Zhejiang, Guangxi, Chongqing, Jiangxi, Hunan, Sichuan, Henan, Hainan, Jiangsu, Hubei, and Shandong. These regions are the primary focus of this study. Observing the temporal and spatial distribution of reported cases, it was found that the number of reported cases is mainly concentrated in southern China (Fig. 8A) and has shown an increasing trend year by year (Fig. 8B).

Data on population and GDP

The population and GDP data are sourced from the National Bureau of Statistics(<https://www.stats.gov.cn/>). This includes the year-end total population and quarterly GDP of each province. The year-end total population data was interpolated to obtain the monthly population for each region, and the quarterly GDP was averaged to derive the monthly GDP. The data indicate that regions with dense populations and high GDP are mainly distributed in southern and coastal areas of China (Fig. 8C-D).

Data on meteorological and mosquito

All meteorological data comes from the website Weather in 241 Countries Worldwide(<https://rp5.ru/>). For provincial-level studies, Select the data from one meteorological station within the jurisdictions of Beijing, Shanghai, Tianjin, and Chongqing, the four directly controlled municipalities; For provinces with more than five prefecture-level administrative regions, the average data from five meteorological stations was used; Since Qinghai and Hainan provinces have no more than five prefecture-level administrative regions, the average data from three meteorological stations were used. Daily data from 130 meteorological stations, collected from February 2005 to December 2019, were utilized. For the analysis within Guangdong Province, the meteorological stations corresponding to nine prefecture-level cities in Guangdong Province (Shenzhen, Guangzhou, Heyuan, Shantou, Yangjiang, Shanwei, Meizhou, Shaoguan, and Zhaoqing) were selected, and the involved meteorological indicators and their processing remained unchanged.

These meteorological indicators include: Average Temperature (T), which is the atmospheric temperature at 2 m above the ground (unit: °C). Minimum Temperature (Tn), which is the lowest temperature in the past period (not exceeding 12 h) (unit: °C). Maximum Temperature (Tx), which is the highest temperature in the past period (not exceeding 12 h) (unit: °C). Dew Point Temperature (Td), which is the temperature at which air becomes

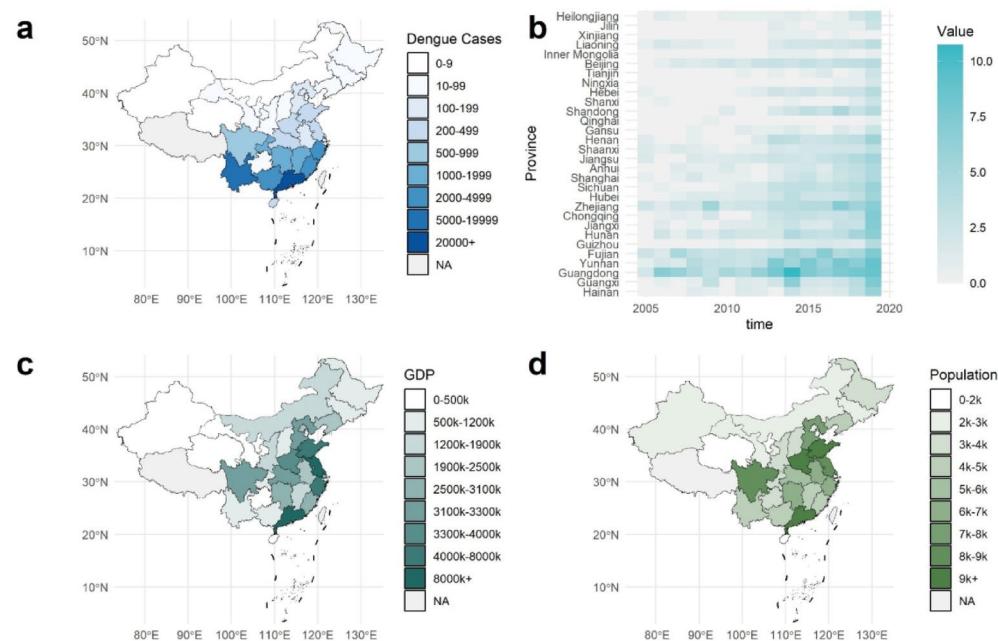


Fig. 8. Spatiotemporal distribution of reported dengue fever cases, population, and GDP Data. **(a)** Cumulative number of reported dengue fever cases in each province from February 2005 to December 2019. **(b)** Annual case counts (log-transformed) of dengue fever for each province from February 2005 to December 2019. Provinces were sorted by latitude from high to low. **(c)** Population of each province as of December 2019. **(d)** Cumulative gross production value for each province from February 2005 to December 2019.

saturated and water vapor begins to condense into dew when cooled (unit: °C). Atmospheric Pressure (P), which is the atmospheric pressure at mean sea level (unit: mmHg). Horizontal Visibility (VV), which is the maximum distance at which an object can be clearly seen and identified in the horizontal direction (unit: km). Precipitation (RRR), which is the amount of rainfall (unit: mm). Relative Humidity (U), which is the relative humidity at 2 m above the ground (unit: %). Wind Speed (Ff), which is the average wind speed at 10–12 m above the ground over the 10 min preceding the observation (unit: m/s). The missing values in meteorological indicators were filled using linear interpolation. Daily precipitation records that were missing, indicated precipitation without measurement, or reported no precipitation have defaulted to 0 millimeters. Time-varying trends of nine meteorological factors were visualized for the 14 provinces with cumulative case numbers exceeding 200 during the study period (see supplementary information Fig.S1–Fig.S14).

The data representing the adult Aedes mosquito population, known as the Mosquito Oviposition Index (MOI), and the data representing the Aedes larvae population, known as the Breteau Index (BI), are sourced from the Guangdong Provincial Health Commission (<https://wsjkw.gd.gov.cn>). The mosquito data for nine prefecture-level cities in Guangdong Province (Shenzhen, Guangzhou, Heyuan, Shantou, Yangjiang, Shanwei, Meizhou, Shaoguan, and Zhaoqing) are selected. According to the monitoring guidelines for dengue vectors published by the Guangdong Provincial Health Commission, monitoring staff establish multiple monitoring points in each city to assess the populations of Aedes mosquitoes, including both *Aedes albopictus* and *Aedes aegypti*. The Guangdong Provincial Health Commission reports monitoring results every half month. These reports detail the proportions of four categories of monitoring points in each city—meeting epidemic prevention and control standards, low-density, medium-density, and high-density areas—with corresponding MOI and BI values for each category. Based on the distribution of monitoring points across different monitoring levels, we can calculate the data of 100 monitoring points for each city. Additionally, we excluded some months that did not report detection results. Furthermore, considering the differences in data reporting methods before 2015 and the potential impact of the COVID-19 pandemic on the population dynamics of Aedes mosquitoes after 2020, the study period was selected from 2016 to 2019 to ensure reliability and accuracy.

Causal analysis

The causal analysis employs a method specifically designed to determine causal relationships in ecological time series—CCM⁵⁸. This method can accurately detect causal relationships between variables in nonlinear dynamical systems. Based on Takens' embedding theorem, the dynamic characteristics of a multidimensional dynamical system can be captured through the time series embedding of a single variable. In CCM, the causal relationship between variables is inferred by assessing whether the historical time series of one variable can reliably predict or explain the state of another variable. That is, in a pair of time series (X, Y) , if Y has higher predictive power for X , then a causal relationship in the direction of $X \rightarrow Y$ can be detected. First, we prepared the state space M_Y reconstructed by the Y 's embedding dimension E_Y . Then, in a leave-one-out manner, we predict X from M_Y using the simplex projection method, labeled as \hat{X}^Y . The Pearson correlation coefficient

between the X and the \widehat{X}^Y , denoted as $\rho_{X \rightarrow Y}^{CCM} = |Corr(X, \widehat{X}^Y)|$, is used to quantify the CCM skill. The CCM skill value approaching 1 indicates that Y can be predicted from X more accurately, which means the causal relationship from X to Y is stronger.

Specifically, the CCM method involves the following steps: First, the optimal embedding dimension is determined using the simplex projection method, where the optimal embedding dimension corresponds to the highest prediction skill. Second, the S-mapping (Sequential Local Weighted Global Linear Mapping) technique is used to test for the presence of nonlinear relationships. Finally, with the optimal embedding dimension and the presence of nonlinear relationships ensured, the CCM skill is calculated. If the CCM skill improves and shows a convergence characteristic as the time series length increases, it can be inferred that there is a causal relationship between the variables. With limited or noisy field data, CCM is demonstrated by an increase in predictability as the time series lengthens. We performed a causal analysis between all meteorological factors and case numbers for the 14 provinces with the highest number of reported cases and also conducted a significance test for the causal relationships.

The causal relationships detected by the CCM method have transitivity, which makes it impossible for us to distinguish whether the causal relationship between factors and case numbers is direct or indirect with intermediate variables. We further used a method that can identify direct and indirect causality, called PCM⁴⁷.

PCM is an extension of CCM. The key idea is to exclude the influence of a third variable when checking the consistency between the cross-mapping predictions of one time series with another. For a direct causal relationship from X to Y, indirectly influenced by Z, this is achieved by calculating the partial correlation

coefficient $\rho_{X \rightarrow Y|Z}^{PCM} = |PCC(X, \widehat{X}^Y | \widehat{X}^{\widehat{Z}^Y})|$. Here, $\widehat{X}^{\widehat{Z}^Y}$ is obtained by a successive simplex projection ($\widehat{X}^{\widehat{Z}^Y}$

is X predicted by $M_{\widehat{Z}^Y}$ where \widehat{Z}^Y is Z predicted by M_Y). When the computed partial correlation coefficient exceeds a given threshold, it is considered that there is a direct causal relationship from X to Y. Based on this, the high-order PCM can be derived as $\rho_{X \rightarrow Y|\{Z_i\}}^{PCM} = |PCC(X, \widehat{X}^Y | \{ \widehat{X}^{\widehat{Z}_i^Y} | i = 1, 2, \dots \})|$. $PCC(x, y|z)$

is the partial correlation coefficient that describes the degree of association between x and y after removing the effect of variable z, $PCC(x, y|z) = \frac{Corr(x, y) - Corr(x, z)Corr(y, z)}{\sqrt{(1 - Corr(x, z)^2)(1 - Corr(y, z)^2)}}$. This definition can be recursively extended to the case where there are multiple intervening variables between X and Y. For example, if there are two intervening variables, Z_1 and Z_2 , the partial correlation coefficient is given

by: $PCC(X, Y|Z_1, Z_2) = \frac{PCC(X, Y|Z_1) - PCC(X, Z_2|Z_1)PCC(Y, Z_2|Z_1)}{\sqrt{(1 - PCC(X, Z_2|Z_1)^2)(1 - PCC(Y, Z_2|Z_1)^2)}}$. If the mediating variable is irrelevant, including it in the partial correlation coefficient formula will not affect the final calculation result.

First, we conducted a PCM analysis on the relationship between meteorological factors and GDP and the number of reported cases in Guangdong Province, which has the highest number of reported cases. Considering that dengue fever is a mosquito-borne disease and previous literature indicates that meteorological factors such as temperature and rainfall can indirectly affect dengue fever by influencing mosquitoes⁵⁹, we also performed a PCM for the average values of meteorological factors, MOI, and BI collected from nine cities in Guangdong Province. According to the concept proposed by Leng and colleagues⁴⁷, we determined whether there is a direct causal relationship between factors, the number of reported cases, and mosquitoes by calculating the partial correlation coefficients and comparing them to a given threshold of 0.4. Additionally, we tested the significance of the PCM values using the t-statistic.

Principal component analysis

PCA was employed to identify more important and representative variables⁶⁰. PCA decomposed the total variance of the 11 original variables x_1, x_2, \dots, x_{11} , denoted as $\sum_{i=1}^{11} D(x_i)$, into the sum of the variances of 11 independent variables y_1, y_2, \dots, y_{11} , denoted as $\sum_{i=1}^{11} D(y_i)$. The contribution rate of the k^{th} principal component y_k is $\phi_k = \frac{\lambda_k}{\sum_{k=1}^{11} \lambda_k}$, where $\lambda_1, \lambda_2, \dots, \lambda_{11}$ are the eigenvalues of the covariance matrix of the original variables. The cumulative contribution rate of the principal components $y_1 \sim y_m$ is denoted as $\psi_m = \sum_{k=1}^m \frac{\lambda_k}{\sum_{k=1}^{11} \lambda_k}$. where $m < 11$. As the rank of the principal components decreases, the amount of original information explained by each principal component diminishes.

Regression analysis

The regression part aims to explore the nonlinear relationship and lag effect between meteorological factors (temperature and pressure) and the number of reported cases in different provinces. To achieve this, a distributed lag nonlinear model (DLNM)⁶¹ combined with a generalized additive model (GAM)⁶² was used to capture the nonlinear effects of meteorological factors and their time-lagged characteristics. Considering the strong correlation between temperature and pressure, separate GAMs were established for temperature and pressure in each province, and GDP was included as a covariate. It is assumed that the number of reported cases follows a Poisson distribution, and a log link function is used to describe the relationship between the predictor variables and the number of reported cases. The average values of the meteorological variables are used as the reference values for calculating relative risks. The model is represented as:

$$\log [E(Y_t)] = \alpha + cb(M) + s(GDP).$$

Y_t is the number of reported cases in month t. $s(\cdot)$ is a natural spline smoothing function. α is the intercept term. M represents meteorological factors: temperature or pressure. $cb(M)$ denotes the cross-basis function, which is obtained using DLNM to model the nonlinear and distributed lag effects of meteorological factors. Based on the comprehensive reference to the lag effects of temperature and pressure from previous research results^{11,27,63–65}, 6 months were chosen as the maximum lag time. When constructing the cross-basis, the lag window was set from 0 to 6 months using the crossbasis() function, and natural splines were used to flexibly estimate the shape of the lag effects. The selection of degrees of freedom was determined by the automatic smoothing selection mechanism in the “mgcv” package in R.

Data availability

All data sources used in this study are publicly available and free. All data and code used in this paper have been made publicly available in a GitHub repository and can be accessed through the following link: <https://github.com/xyyu001/CCM14>.

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Author contributions

Xingyuan Yu: Writing – original draft, Validation, and Data curation. Xia Wang: Writing – review & editing, Software, and Methodology. Sanyi Tang: Investigation and Funding acquisition. All authors have read and approved the final manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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Correspondence and requests for materials should be addressed to X.W.

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