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Predicting the risk of malaria importation into Jiangsu Province, China: a modeling study

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Abstract

Background The World Health Organization certified China malaria-free in 2021. Consequently, preventing the risk of malaria re-introduction caused by imported malaria has now become a major challenge. This study aims to characterize the dynamics and predict the risk of malaria importation in Jiangsu Province, where the number of imported malaria cases ranks among the highest in China.

Methods The annual number of cases with imported malaria in Jiangsu Province, the annual number of travelers from sub-Saharan Africa (SSA) to Jiangsu Province (both Chinese and international travelers), and the annual number of Chinese migrant workers from Jiangsu Province who stayed abroad between 2013 and 2020 were assessed. The spatio-temporal dynamics of malaria importation was characterized with ArcGIS 10.8. A negative binomial model was applied to model malaria importation to Jiangsu Province, China.

Results A total of 2,221 of imported malaria cases were reported from January 1, 2013, until December 31, 2020. Imported malaria cases into China were mainly from SSA (98%) and *P. falciparum* (78%), the most common species. A seasonal pattern was observed, with the most cases occurring from December to February. The negative binomial model, which incorporates the number of Chinese migrant workers from Jiangsu Province who stayed abroad as an independent variable, demonstrated better performance (AIC: 96.495, BIC: 94.230) compared to the model based solely on travelers from SSA to Jiangsu Province. The model indicated an estimated 139% increase in imported cases for a 10% increase in Chinese migrant workers from Jiangsu Province who stayed abroad.

Conclusion In conclusion, our study underscores the importance of incorporating data on Chinese migrant workers who have stayed abroad when predicting malaria importation risks. By integrating both international travel patterns and migrant worker data, our findings offer a more robust framework for assessing and managing malaria risk in Jiangsu Province. This approach provides valuable insights for public health officials, enabling more effective resource allocation and targeted interventions to prevent the re-introduction of malaria and improve overall disease management.

Keywords Imported malaria, Prevention of malaria reintroduction, Migrant workers, Travel medicine, Malaria elimination

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Introduction

Although half of the countries in the world have eliminated malaria in the past 150 years, malaria remains one of the deadliest infectious diseases worldwide. It represents a major public health problem globally [1, 2]. The epidemiology of malaria in countries that have achieved elimination has now become more complex as malaria becomes increasingly imported [3, 4]. Malaria reintroduction through imported cases has already been observed in Greece [5, 6], Italy [7] and America [8], thus remains a significant challenge [5–10].

Malaria has been a major public health problem in China in the recent past, with the great majority of the population in China having been at risk of infection and with some 30 million cases annually reported during the 1940s [11]. Following continued and comprehensive efforts to control malaria, China had launched the National Malaria Elimination Program (NMEP) in May 2010 [12] and was certified by the World Health Organization (WHO) as malaria-free on June 30 2021 [13–15]. However, the rapid growth of Chinese overseas travel and the increasing investment in international projects have led to frequent exchanges of domestic and international personnel, resulting in a rise in the number of imported malaria cases [16–19]. Therefore, maintaining a robust public health infrastructure for the surveillance of travel-associated malaria and developing innovative strategies to prevent the reintroduction of malaria is essential [20]; however, there is a lack of evidence regarding this phase and the risk groups for imported malaria.

Studies have demonstrated that imported cases of malaria in China are mainly due to Chinese migrant workers returning from malaria-endemic regions, which contrasts with the situation in the USA and Europe, where malaria is often imported by citizens with migration backgrounds after having visited friends or relatives in their country of origin or through tourists [21]. In malaria-endemic countries, Chinese migrant workers mainly work outdoors and generally are particularly vulnerable to malaria acquisition [22–26]. Understanding the dynamics of malaria infection in this population plays a vital role in strengthening the malaria surveillance systems, which is considered the most critical tool in the prevention of malaria re-introduction.

The relationship between air travel and importation risk has been modeled for many other infectious diseases, including MERS, chikungunya, dengue, Zika, Ebola, Lassa fever, and COVID-19 [27–34]. However, the relationships between the number of imported malaria, travel data, and indices of importation have not been investigated much. Therefore, our study aims to (1) document the spatio-temporal pattern of malaria importation to Jiangsu Province from 2013 to 2020, (2) investigate the association between the annual number of Chinese migrant workers staying abroad and the risk of malaria importation to Jiangsu Province, and (3) investigate the association between the annual number of travelers from sub-Saharan Africa (SSA) and the risk of malaria importation to Jiangsu Province.

Methods

Study setting

Jiangsu Province is in southeastern China and has an area of 102.6 thousand square kilometres (Fig. 1A) [35].

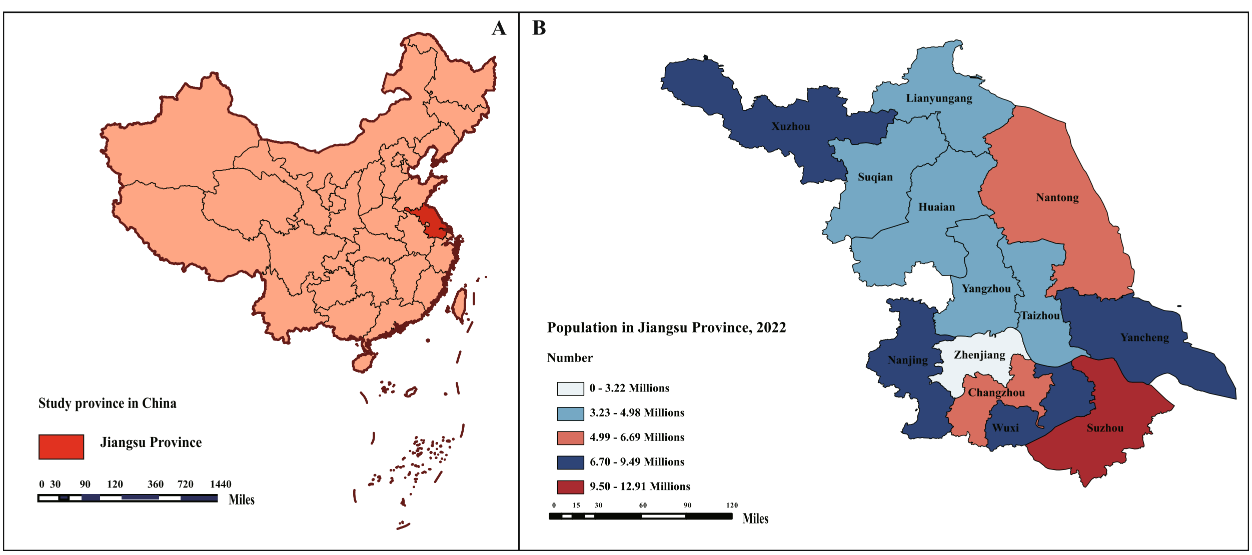

Fig. 1 The location of Jiangsu Province in southeastern China, along with other provinces (**A**) and the geographical distribution of the permanent population in Jiangsu Province in 2022, is shown (**B**)

In Jiangsu Province, there are 13 prefecture-level cities, and the permanent population reached 85.15 million by the end of 2022 (Fig. 1B) [36]. Regarding the number of imported malaria cases, Jiangsu Province has consistently ranked among the highest in China, with an annual number ranging from 90 to 405 between 2013 and 2020 [37]. Moreover, the GDP of Jiangsu Province ranked second in China in 2022, and it is one of the most prosperous provinces in China [36, 38]. It is also one of the leading provinces in sending Chinese migrant workers to work abroad, with an average annual count exceeding 20,000 [39].

Diagnosis and reporting of imported malaria

In China, the following criteria for the definition of imported malaria must be met simultaneously: (i) the patient was laboratory-diagnosed with malaria: malaria parasites confirmed by microscopy, a positive rapid diagnostic test (RDT), or a positive polymerase chain reaction (PCR) test, regardless of the presence of typical malaria symptoms [40], (ii) the patient had a travel history to malaria-endemic areas outside of China during the malaria transmission season, and (iii) the onset of malaria occurred < 1 month after returning to China during the local transmission season [41, 42]. The case was classified as local if any of the above criteria were not met. Disagreements regarding any case classification had to be resolved during routine meetings by provincial or national experts. We selected data from 2013 to 2020 due to the significant improvements in the malaria surveillance system that were implemented from 2012 onwards, which ensured the accuracy and completeness of data on imported malaria [16]. The data on number of cases with imported malaria in the 13 prefectures of Jiangsu Province were collected from the web-based *China Information System for Disease Control and Prevention* (http://www.phsciencedata.cn/), a real-time, web-based infectious disease surveillance and response system [43]. Due to the strict regulations implemented by the Chinese Center for Disease Control and Prevention (CDC) to protect patient privacy, permission is required for access to and use of these data.

Global spatial autocorrelation analysis

The number of cases with imported malaria at the prefecture level in Jiangsu Province was plotted annually using GIS mapping [44]. The annual number of imported cases at the prefecture-level for each year was determined to assess the spatial distribution of imported malaria. The digital map of Jiangsu Province at the prefecture-level was obtained from the *Data Sharing Infrastructure of Earth System Science* (http://www.geodata.cn/). The global spatial autocorrelation was investigated using Global Moran's I statistics in ArcGIS software version 10.8 (ESRI Inc., Redlands, CA). Moran's I statistical analysis tests the null hypothesis that measures the values at a location independent of values at other locations. The values vary from -1 to 1. Positive (negative) values indicate the presence of positive (negative) spatial autocorrelation, whereas a zero value indicates a random spatial pattern [45].

Spatial clustering analysis

Local spatial autocorrelation analyses the heterogeneity domain and finds concealed abnormal values, unlike what global spatial autocorrelation finds. The spatial clustering of imported malaria was performed using Anselin's Local Moran's I to identify the high-risk areas in ArcGIS software [46]. Anselin's Local Moran's I [47] detected of spatial autocorrelation between a city and its adjacent city. The weight element was assumed to be one of two cities were neighbours; otherwise, we assumed if two cities were neighbors; otherwise, we assumed the value was 0 in the weight matrix, which defines the spatial autocorrelation among cities. Spatial clusters of imported malaria were identified by detecting local areas where cities with a high number of borders to other cities with a high number of imported cases with malaria (high–high pattern) and where cities with a high number border cities with a low number of imported cases with malaria (high–low pattern). Local indicators of spatial association (LISA) cluster maps were used to explore the spatial cluster types and specific cluster locations of diseases in the study area.

Variables considered in modelling the importation of malaria

Our dataset encompasses annual data from 2013 to 2020, including: (1) the year of reporting imported malaria; (2) the city of reporting; (3) the number of imported malaria cases; (4) malaria species; (5) travelers' continent of origin; (6) travelers' country of origin; (7) travelers' arrival year; (8) the number of travelers; (9) the city of origin of Chinese migrant workers who stayed abroad; (10) the year of stay abroad; and (11) the number of such migrant workers.

Travelers from SSA to Jiangsu Province

The travelers information includes arriving time, continent and country of origin were available from the Jiangsu Provincial Bureau of Statistics (http://tj.jiangsu.gov.cn/) [48]. Data on travelers from SSA to Jiangsu Province between 2013 and 2020 are collected anonymously and aggregated by year and province. These travelers, including foreigners and overseas Chinese visiting for purposes such as sightseeing, family reunions, vacations, conferences, business, or education, were recorded [36, 48]. However, data on the annual number of travelers from SSA were available only up to 2012. To estimate traveler numbers for 2013 to 2020, we averaged the proportions from previous years and applied weighted proportions based on the total number of travelers each year [49].

Annual number of Chinese migrant workers from Jiangsu Province who stayed abroad

Data on the annual number of Chinese migrant workers from Jiangsu Province who stayed abroad from 2013 to 2020 were obtained from the Department of Commerce of Jiangsu Province (http://doc.jiangsu.gov.cn/) [50]. According to the Ministry of Commerce of China's definition, Chinese migrant workers who stayed abroad were counted by enterprises as the number of individuals who went abroad through export labor companies and worked as overseas laborers at the end of each year [51].

Quantifying the risk of malaria importation

In comparison to the Poisson regression model, the negative binomial regression does not assume equidispersion and is suitable for overdispersed data, where the variance exceeds the mean. Testing for equidispersion [52, 53] revealed that the data on imported malaria cases exhibited overdispersion (mean: 277.6, variance: 9449.7). Thus, a negative binomial regression model was employed to account for this overdispersion. Given the high annual counts of passengers and workers, a logarithmic transformation was applied to stabilize variance [28, 54, 55]. The main predictors were the log-transformed number of travelers from SSA to Jiangsu Province and the annual number of Chinese migrant workers who stayed abroad and the dependent variable was the annual number of imported malaria cases in Jiangsu Province. Overall model significance was evaluated using the omnibus test, while the Wald Chi-Square test was used to assess the significance of individual parameters. Significance was tested at an α level of 0.05, with non-significant variables excluded from the multivariable model. Model performance was compared using the Akaike Information Criterion (AIC) and the Bayesian Information Criterion (BIC), where lower values indicate a better fit [56]. All analyses were conducted using *R* (version 4.2.2).

Results

Epidemiological characteristics of imported malaria

Between 2013 and 2020, 2,221 cases with imported malaria were reported in Jiangsu Province, peaking in 2015 ($n=405$). The annual number slightly decreased in recent years, particularly during 2020 (Fig. 2). SSA was the most common region of origin (98%, 2,169/2,221). *Plasmodium falciparum* was the dominant species,

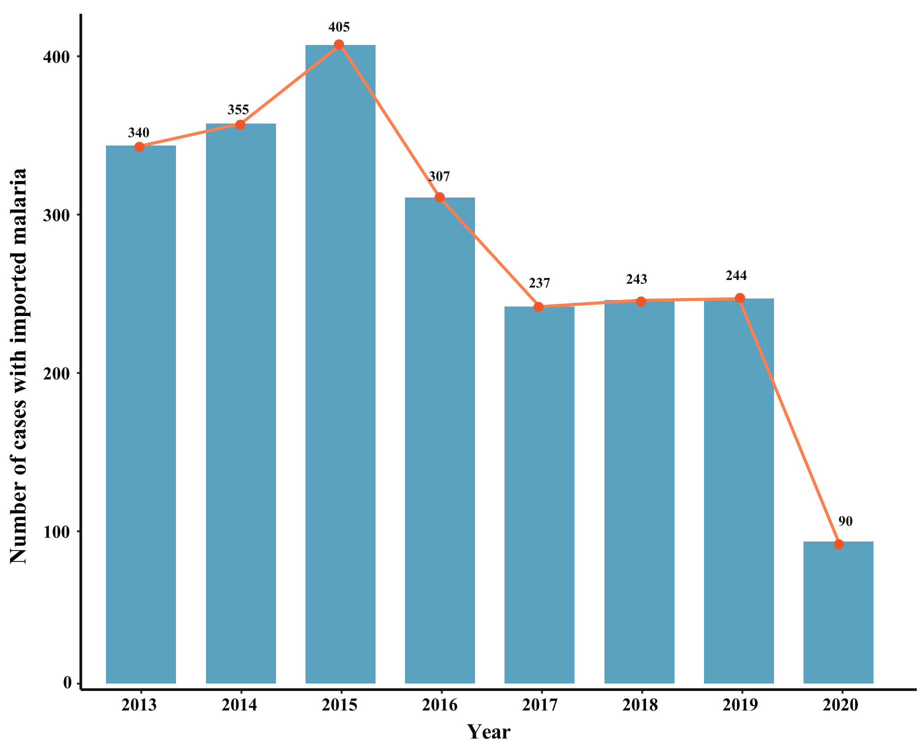

Fig. 2 Epidemic curves of cases with imported malaria in Jiangsu Province, China, 2013–2020

accounting for 78% (1,728/2,221) of the total imported cases, followed by *Plasmodium ovale* (13%, 289/2,221) and *Plasmodium vivax* (5%, 113/2,221). In terms of the purpose of traveling from 2013 to 2019, 93.01% (1,982/2,131) of the patients were migrant workers, 3% (69/2,131) were business travelers, and 2% (41/2,131) were students. Figure 2 shows that there were cases with imported malaria throughout the year.

Seasonal pattern of cases with imported malaria

The seasonal pattern concerning the number of cases with imported malaria between 2013 and 2020 was consistent over time (Fig. 3A). Imported malaria cases occurred all over the year. Still, December–February was the peak time for cases across the eight year observation period (30%, 670/2,221), while January was the peak month for *P. falciparum* and *P. vivax* and February and September with proportions of 15% (252/1,728) and 14% (16/113), respectively.

Spatio-temporal analysis of cases with imported malaria

The dynamic of cases with imported malaria in Jiangsu Province is shown in Fig. 4. Nearly all 13 prefecture-level cities in the province reported imported malaria between 2013 and 2020. Central Jiangsu Province has continuously reported the most significant number of imported cases (838/2,221, 38%), followed by the northern region with 831 (37%) and the southern region with 552 (25%). Although Taizhou City reported the largest, most significant number of annual cases of imported malaria in 2015, Nantong City, which is located in central Jiangsu Province, reported the most significant number of cases from 2013 to 2020. A total of 335 cases were reported in Nantong city, accounting for 15% of the total cases with imported malaria in Jiangsu Province. Moreover, the spatial cluster analysis showed that the distribution of cases with imported malaria was not random in the study area and found that only one high–high cluster city was Nantong city in 2017 (Fig. 5).

Modeling of malaria importation dynamics

Potential predictors

From 2013 to 2020, there were 303,893 travelers from SSA to Jiangsu Province and 721,327 Chinese migrant workers from Jiangsu who stayed abroad. On average, nearly 40,000 SSA travelers visited Jiangsu annually, while about 90,000 Chinese migrant workers stayed abroad each year. The number of SSA travelers to Jiangsu grew continuously from 2013, peaking in 2019 (Fig. 6). The number of Chinese migrant workers abroad increased steadily from 2013 to 2015, experienced a slight decline in 2016, and then rose again, peaking in 2018 (Fig. 6).

Model one: prediction of malaria importation based on travelers from SSA

The negative binomial model demonstrated a statistically significant relationship between the log of the annual number of travelers from SSA to Jiangsu Province and the risk of detecting cases with imported malaria ($P < 0.05$) (Table 1). According to this model, we found that a 10% increase in the volume of travelers from SSA to Jiangsu Province was associated with a 106% increase in the number of cases with imported malaria (Table 2).

Model two: prediction of malaria importation based on the annual number of Chinese migrant workers stayed abroad

The coefficient of the annual number of Chinese migrant workers from Jiangsu Province who stayed abroad, which predicted the risk of cases with imported malaria, was

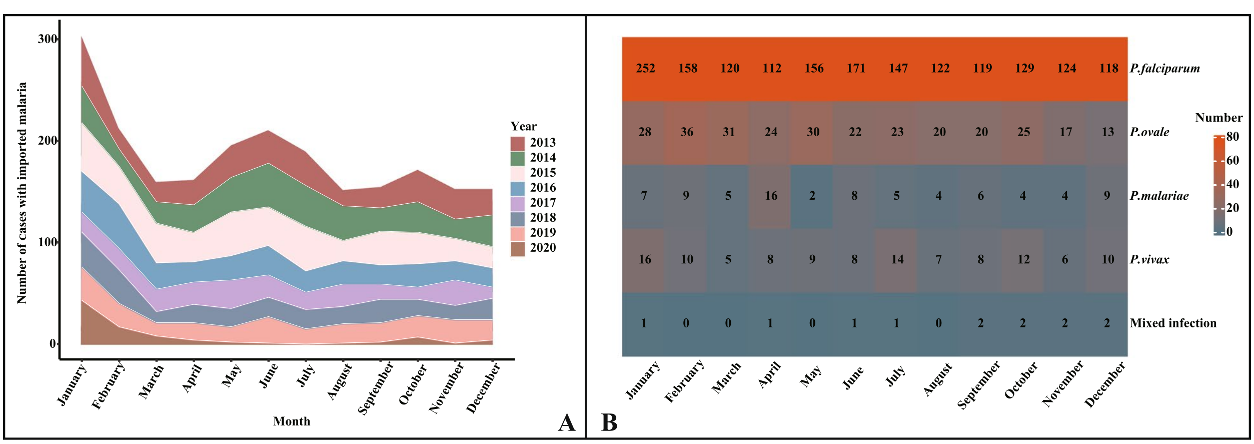

Fig. 3 The seasonal pattern of cases with imported malaria in Jiangsu Province, China, from 2013 to 2020 (**A**); The temporal distribution of cases with imported malaria by *Plasmodium* species reported in Jiangsu, China, from 2013 to 2020 (**B**)

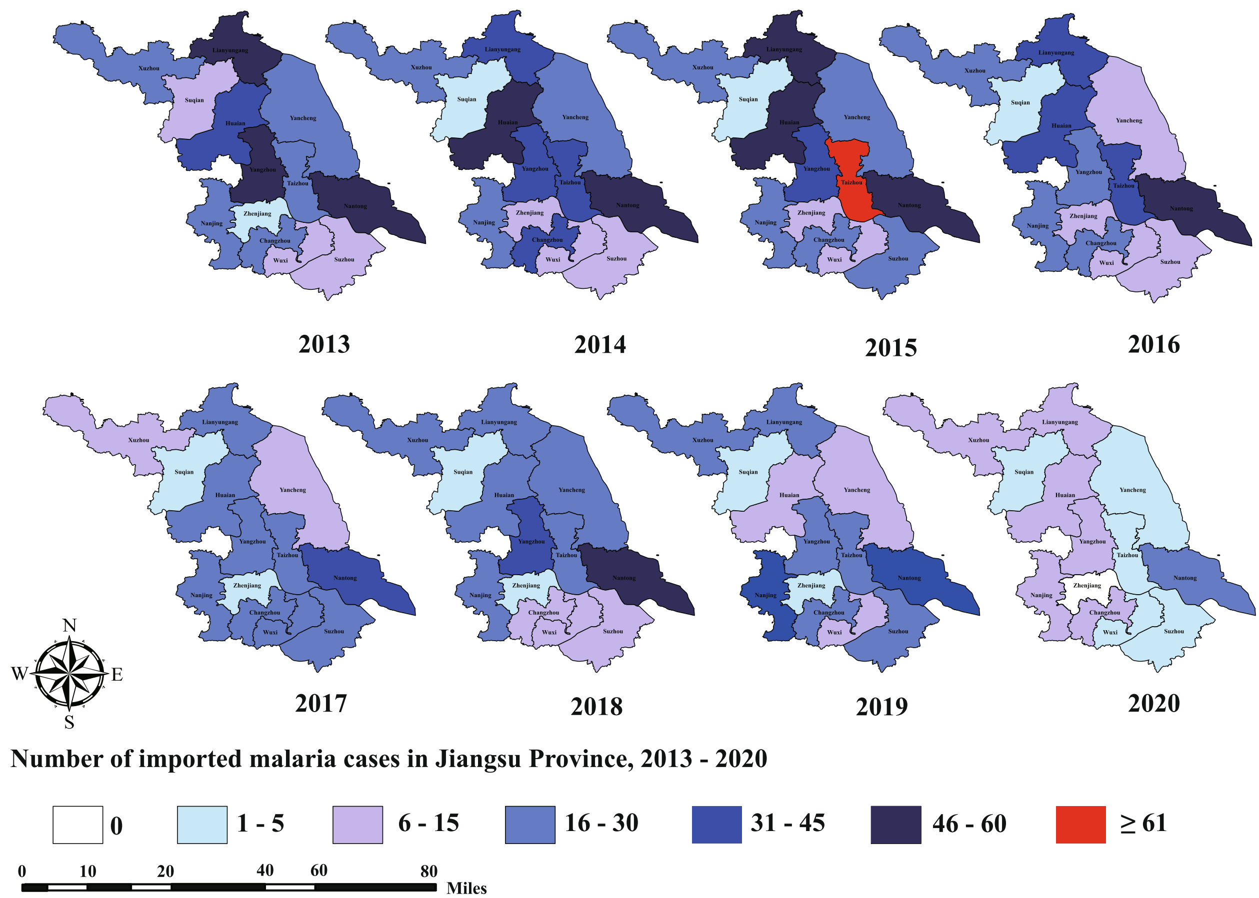

Fig. 4 Spatio-temporal distribution of cases with imported malaria in Jiangsu Province, 2013–2020

statistically significant at the 5% level (Table 1). Model two showed that a 10% increase in the volume of Chinese migrant workers from Jiangsu Province who stayed abroad was associated with a 139% increase in cases with imported malaria (Table 2).

The log-likelihood ratio test found that the fit of Model Two (likelihood value = −44.00) was better than the fit of Model One (likelihood value = −45.40), Likelihood ratio test $\chi 2 = 2.80$, $P < 0.001$. The Model Two had smaller deviance (Model Two: 7.95 vs. Model One: 8.03), larger Log likelihood (Model Two: −87.99 vs. Model One: −90.79).

Model performance

The likelihood ratio test revealed that overdispersion in the data of cases with imported malaria was present in the null model; therefore, the negative binomial regression model was applied. The dispersion parameters (Model One: $\theta = 9.96$; Model Two: $\theta = 14.91$) showed that the mean was less than the variance, which indicated a good fit of the negative binomial regression model. Furthermore, based on the AIC and BIC, we found that Model Two (AIC = 96.495, BIC = 94.230) marginally outperformed Model One (AIC = 99.755, BIC = 97.033) (Table 1).

Discussion

In this study, we revealed the changing pattern of malaria importation to Jiangsu Province from 2013 to 2020. We developed two models of malaria importation based on travelers from SSA and Chinese migrant workers who stayed abroad. We also demonstrated some seasonality of the imported malaria cases. We highlighted the value of the annual number of Chinese migrant workers who stayed abroad in predicting the number of imported malaria cases to China. By better knowing the risk of the importation of malaria in the province as a whole and which specific cities should be more concerned, the public health workers and policy-makers could strengthen and better allocate human resources to improve the case management of cases with imported malaria and prevention of malaria-introduction.

The results of this study further that the health management of Chinese migrant workers should be strengthened to ensuring the prevention of malaria

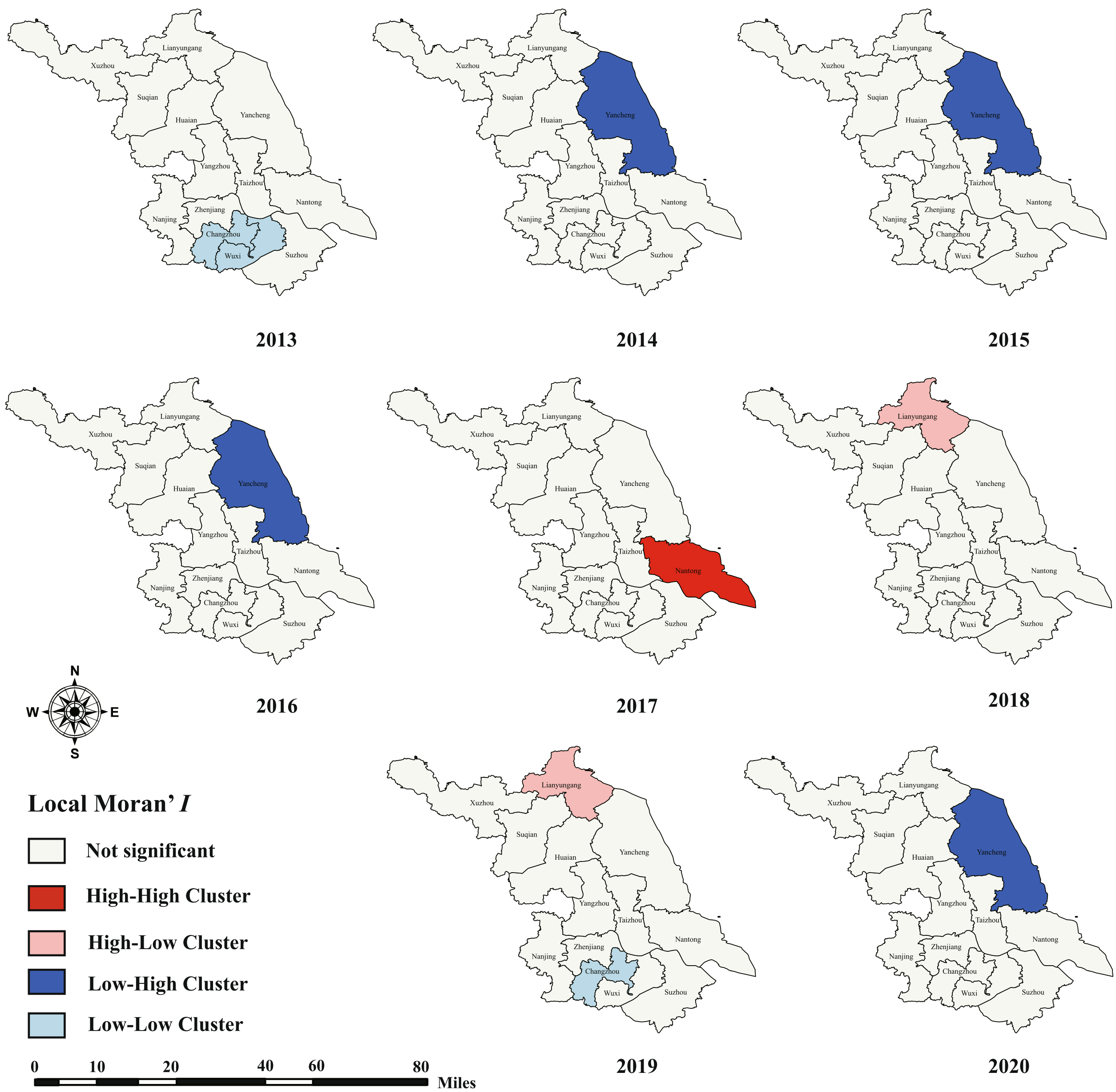

Fig. 5 Annual LISA map of cases with imported malaria from 2013 to 2020. Changzhou and Wuxi city were identified as low–low cluster cities from 2013 to 2020. Yancheng city was identified as a low–high cluster city from 2014 to 2016 and in 2020. Lianyungang city was recognised as a high–low city in 2018 and 2019. The only high–high cluster city in 2017 was Nantong city

re-introduction. With the rapid development of international economic exchange and travel, the number of international migrant workers has increased mainly in recent decades [22]. According to statistics from the United Nations Tourism (UN Tourism), approximately 66.36 million travelers visited the African region in 2023 [57]. This marks an increase of 41.28% from 46.97 million in 2022. It is estimated that the number of Chinese migrant workers who went abroad reached 258,826 by 2022, 11% of whom went to SSA [58]. Chinese migrant workers are mainly involved in outdoor activities such as infrastructure construction or mining [19, 41, 59], and they are generally susceptible to malaria infection at their destination [60]. In addition, the workers typically lack awareness of the importance of early care-seeking and prompt use of health-care services after infection [61, 62]. The hot cities identified in this study was consistent with previous studies reporting a significant higher delayed care-seeking among migrant workers with imported malaria

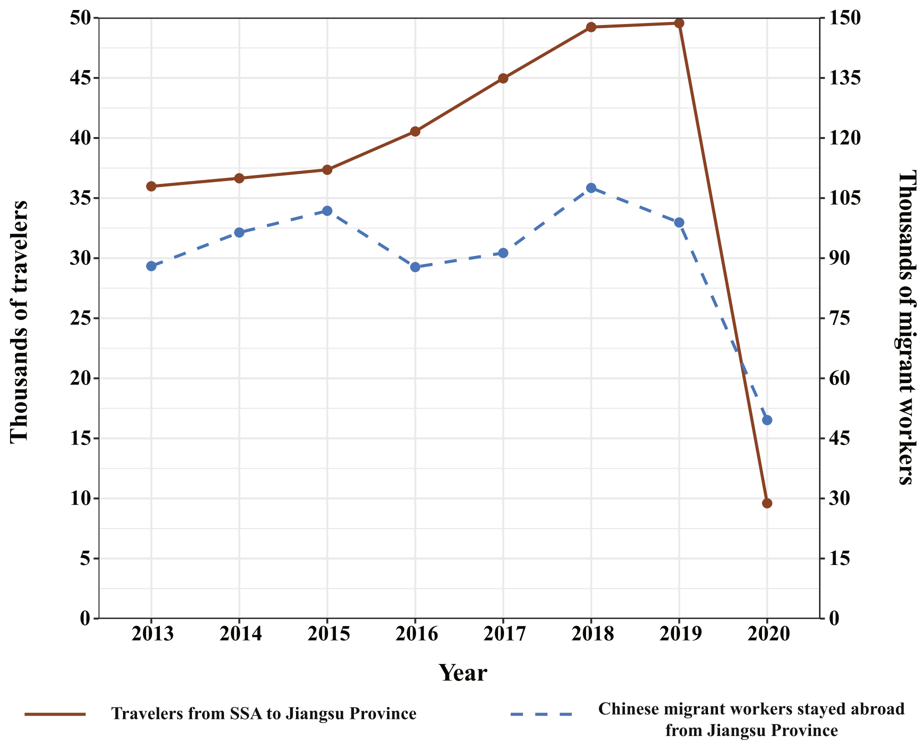

Fig. 6 Total number of travelers from SSA to Jiangsu Province (left axis) and Chinese migrant workers from Jiangsu Province who stayed abroad (right axis) from 2013 to 2020

Table 1 Summary of the results of a multivariable negative binomial regression model for predicting cases with imported malaria

Model	Variable	Coefficient	*Z*	*P*	Standard errors	AIC	BIC	*θ*
Model One	Intercept	2.731	2.062	0.039	2.068	99.755	97.033	9.96
	Log of travelers from SSA to Jiangsu Province	0.616	2.178	0.029	0.454			
Model Two	Intercept	−9.948	−2.304	0.021	4.230	96.495	94.230	14.91
	Log of Chinese migrant workers stayed abroad from Jiangsu Province	3.274	3.600	0.000	0.855			

Table 2 Prediction of the increase in the number of cases with imported malaria based on the increase in the volume of travelers from SSA to Jiangsu Province (Model One) or Chinese migrant workers who stayed abroad from Jiangsu Province (Model Two), based on negative binomial models and aggregated by year

Model	Increase in annual volume of predictors	Increase in cases with imported malaria with 95% confidence interval
Model One	1%	100.1% (100.0%, 101.3%)
	5%	103.1% (99.9%, 106.8%)
	10%	106.3%(99.8%, 114.0%)
Model Two	1%	103.3% (101.2%, 105.3%)
	5%	117.8% (106.3%, 129.4%)
	10%	138.7% (112.9%, 167.4%)

[62]. Thus, ensuring the timely diagnosis and treatment of migrant workers with imported malaria is crucial for reducing morbidity and mortality, as well as for prevention of malaria re-introduction. This can be achieved by maintaining and enhancing diagnostic capabilities within medical facilities and promoting care-seeking behaviors following the onset of symptoms.

To our knowledge, this is the first study which quantifies the association between the number of Chinese migrant workers who stayed abroad and the number of cases with imported malaria, considering that people with imported malaria in China are mainly Chinese migrant workers returning from SSA [22, 61]. International travel data have been primarily used to predict the incidence of infectious diseases, including chikungunya, dengue fever, yellow fever and malaria [28, 63–67]. For example, Findlater et al. showed that a 10% increase in air travel is associated with only a 6% increase in the number of imported dengue fever cases in China [28]. Nasserie et al. showed that as the number of arriving airline passengers increased by 10%, the estimated number of imported chikungunya cases increased by 5% in the USA [63]. Interestingly, our study demonstrated the importance of incorporating data on Chinese migrant workers who have stayed abroad when predicting malaria importation risks.. These findings further indicated the importance of considering demographic and epidemiological changes in modelling of infectious disease importation.

The observed seasonal pattern, with the peak timing of the presentation of cases with imported malaria in December–February in this study, exactly reflects the increased movement in international and domestic populations during the *Spring Festival* holiday in China [68]. Such similar seasonal variations in the numbers of cases with imported malaria have also been reported from other countries, for example, the peak season for imported malaria cases in Nepal is after the monsoon season [69]. Delayed healthcare seeking of patients and thus delayed diagnosis may also increase during festivals, which may be explained by traditional beliefs and habits, and behavior during public holidays. This further indicates the importance of increasing public health vigilance with regarding the prevention and early detection of cases with imported malaria during local festivals.

Our study further highlights that innovative methods are needed to strengthen the surveillance system for imported malaria to prevent malaria re-introduction. Globally, the *GeoSentinel Surveillance Network* [70] and *European Network for Tropical Medicine and Travel Health* (TropNet) [71] are the most crucial international surveillance networks for accurately measuring the incidence of health problems among travelers [72]. Similarly, in China, since the launch of the Malaria Elimination Initiative in 2010, China initialized the malaria '1–3–7'surveillance and response system to further strengthen the capacity to detect and investigate each malaria case promptly [42, 73]. Specifically, China's '1–3–7' malaria surveillance and response approach was developed, including case reporting within one day, case investigation within three days and focus/foci investigation and action within seven days in early 2012 [42]. More importantly, the working scheme of China's '1–3–7' approach was seen to be successfully integrated with surveillance of other travel-associated infectious diseases, such as COVID-19 [74]. Such a continually improving surveillance and response system could play a critical role in the early detection of and rapid response to individual malaria cases. It could help to prevent the re-establishment of malaria.

Public health policy implications

Our study highlights the evolving patterns of malaria importation to Jiangsu Province from 2013 to 2020 and underscores the importance and feasibility of utilizing data on both travelers from SSA or Chinese migrant workers who stayed abroad to predict the risk of malaria importation to China. Given the identified seasonality in malaria cases, public health efforts should be timed and tailored accordingly. By focusing on the annual number of returning migrant workers, policymakers can more accurately predict and manage the risk of malaria importation. Enhanced resource allocation and targeted interventions in high-risk cities could improve case management and prevent malaria re-introduction.

There are some limitations to this study. First, we exclusively assessed international travelers from SSA to Jiangsu Province in this study, considering no regions of origin; however, more than 95% of cases with imported malaria reported in Jiangsu Province resulted from *P. falciparum* from SSA, and very few cases were from Southeast Asia. Second, the international travelers to Jiangsu Province reported by the Jiangsu Provincial Bureau of Statistics only include overseas returnees from SSA who spend at least one night in Jiangsu Province. Consequently, our data may not encompass short-stay travelers to Jiangsu Province, such as transfer passengers and airline crew members. Third, the number of migrant workers who stayed abroad included workers who stayed on continents other than Africa, and there is no detailed information available. However, cases of imported malaria were mainly found in migrant workers returning from SSA. Fourth, while seasonality is evident in the imported cases, with a peak from December to January, most likely corresponding to the seasonality of the return of migrant workers, we did not incorporate this seasonality in our analysis. Finally, future studies may consider establishing a correlation between comprehensive determinants, along with other factors such as vectorial capacity aspects, to predict the risk of malaria re-introduction in China.

Conclusions

In conclusion, our study underscores the importance of incorporating data on Chinese migrant workers who have stayed abroad when predicting malaria importation risks. By integrating both international travel patterns and migrant worker data, our findings offer a more robust framework for assessing and managing malaria risk in Jiangsu Province. This approach provides valuable insights for public health officials, enabling more effective resource allocation and targeted interventions to prevent the re-introduction of malaria and improve overall disease management.

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Not applicable.

Authors' contributions
G.Y.L.: study conception and its design; K.X.L., Y.Y.C., J.Z., Y. W., E.Y.X. and Z.Y.C.: data collection; K.X.L., L.Y.C., Y.W., Y.H.X. and O.M.: data analysis and interpretation; K.X.L., Y.Y.C., and G.Y.L.: wrote the draft of the manuscript; J.C. and O.M.: commented on an early version of the manuscript; G.D.Z. and G.Y.L.: revised the manuscript for important academic content.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
All data were supplied and analyzed in an anonymous format, without access to personal identifying information.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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