Journal of Travel Medicine, 2024, taae021
https://doi.org/10.1093/jtm/taae021
Original Article

Original Article

Delayed care-seeking in international migrant workers with imported malaria in China

Jiyue Gu, BSMed[1,†], Yuanyuan Cao, MPH[2,3,†], Liying Chai, MS[1,†], Enyu Xu, MS[1], Kaixuan Liu, MS[1], Zeyin Chong, MS[1], Yuying Zhang, MS[1], Dandan Zou, MS[1], Yuhui Xu, MPH[4], Jian Wang, MPH[5], Olaf Müller, PhD[6], Jun Cao, PhD[2,3], Guoding Zhu, PhD[2,3] and Guangyu Lu, PhD[1,7,*]

[1]Department of Epidemiology and Biostatistics, School of Public Health, Medical College of Yangzhou University, Yangzhou University, Yangzhou, Jiangsu Province, 225009, China, [2]National Health Commission Key Laboratory of Parasitic Disease Control and Prevention, Jiangsu Provincial Key Laboratory on Parasite and Vector Control Technology, Jiangsu Institute of Parasitic Diseases, Wuxi, Jiangsu Province, 214064, China, [3]Center for Global Health, School of Public Health, Nanjing Medical University, Nanjing, Jiangsu Province, 211166, China, [4]Center for Disease Control and Prevention, Yangzhou, Jiangsu Province, 225007, China, [5]Yangzhou Schistosomiasis and Parasitic Disease Control Office, Yangzhou, Jiangsu Province, 225007, China, [6]Institute of Global Health, Medical School, Ruprecht-Karls-University Heidelberg, Heidelberg, 69117, Germany and [7]Jiangsu Key Laboratory of Zoonosis, Yangzhou, 225009, China

*To whom correspondence should be addressed. Email: guangyu.lu@yzu.edu.cn

†Jiyue Gu, Yuanyuan Cao, and Liying Chai contributed equally to this work.

Submitted 25 October 2023; Revised 12 December 2023; Editorial Decision 31 January 2024; Accepted 8 February 2024

Abstract

Background: Imported malaria cases continue to pose major challenges in China as well as in other countries that have achieved elimination. Early diagnosis and treatment of each imported malaria case is the key to successfully maintaining malaria elimination success. This study aimed to build an easy-to-use predictive nomogram to predict and intervene against delayed care-seeking among international migrant workers with imported malaria.

Methods: A prediction model was built based on cases with imported malaria from 2012 to 2019, in Jiangsu Province, China. Routine surveillance information (e.g. sex, age, symptoms, origin country and length of stay abroad), data on the place of initial care-seeking and the gross domestic product (GDP) of the destination city were extracted. Multivariate logistic regression was performed to identify independent predictors and a nomogram was established to predict the risk of delayed care-seeking. The discrimination and calibration of the nomogram was performed using area under the curve and calibration plots. In addition, four machine learning models were used to make a comparison.

Results: Of 2255 patients with imported malaria, 636 (28.2%) sought care within 24 h after symptom onset, and 577 (25.6%) sought care 3 days after symptom onset. Development of symptoms before entry into China, initial care-seeking from superior healthcare facilities and a higher GDP level of the destination city were significantly associated with delayed care-seeking among migrant workers with imported malaria. Based on these independent risk factors, an easy-to-use and intuitive nomogram was established. The calibration curves of the nomogram showed good consistency.

Conclusions: The tool provides public health practitioners with a method for the early detection of delayed care-seeking risk among international migrant workers with imported malaria, which may be of significance in improving post-travel healthcare for labour migrants, reducing the risk of severe malaria, preventing malaria reintroduction and sustaining achievements in malaria elimination.

Key words: Imported malaria, international migrant workers, delayed care-seeking, prevention of malaria reintroduction, China

Background

Although >50 countries have succeeded in eliminating malaria in the past century, it remains a major public health problem worldwide, with 84 countries still being endemic.[1] Moreover, the global achievements could be fragile, particularly in countries where social and economic conditions were disrupted during the coronavirus disease 2019 (COVID-19) pandemic.[2–4] For example, the number of malaria cases increased from 227 million in 2019 to an estimated 241 million in 2020 globally.[1] Therefore, countries certified by the World Health Organization (WHO) as malaria-free should make concerted efforts to prevent the re-establishment of malaria transmission.[5]

China was certified as malaria-free by WHO on 30 June 2021, a remarkable achievement and the culmination of decades of dedicated effort by the national malaria programme and its partners.[6–8] However, imported malaria will remain a threat to China's malaria-free status until global malaria eradication is reached.[9] Imported cases of malaria in China are mainly due to Chinese labourers returning from malaria-endemic regions, which is in contrast to the situation in the USA and in European countries, where malaria is often imported by citizens with migration backgrounds after having visited friends or relatives in their country of origin.[10,11] Therefore, the international community has acknowledged the importance of developing innovative strategies to strengthen and maintain a robust public health infrastructure for the surveillance of travel-associated malaria and to prevent reintroduction[12]; however, there is a lack of evidence regarding this phase and the risk groups of imported malaria.

One major challenge in the case management of imported malaria cases is that malaria is an infrequently encountered disease in areas where malaria has been eliminated, which can delay diagnosis and result in high mortality and secondary local transmission.[13,14] The delay is partly due to the patient (e.g. not seeking healthcare promptly) and partly due to delays caused by medical practitioners (e.g. not asking for a travel history).[15] Great efforts have usually been invested in training general health service providers to maintain their vigilance for early malaria suspicion and diagnosis.[16] However, care-seeking delays among patients with imported malaria have been less investigated, and interventions to promote early post-travel healthcare are often hard to implement.

The care-seeking timing among indigenous malaria patients is influenced by various factors, including personal demographic factors, such as age, sex, education level, income and place of residence.[17–20] However, there is very limited information about delayed post-travel care-seeking in hard-to-reach international migrant workers. Therefore, the aim of the current study was to (i) identify the factors influencing the care-seeking delays among imported malaria patients in Jiangsu Province, which has reported the highest number of Chinese migrant workers with imported malaria returning from malaria-endemic regions in recent decades; (ii) develop a nomogram model to predict the risk of care-seeking delays in patients with imported malaria and (iii) establish and compare the performance of machine learning-based models, including the multilayer perceptron model (MLP), linear support vector machine (LSVM), random forest (RF), logistic regression (LR) and Bayesian model in the prediction of care-seeking delays among patients with imported malaria. These findings may contribute to the development innovative interventions for improving the post-travel healthcare of imported malaria patients and thus the prevention of the re-establishment of malaria.

Methods

Study setting

The study was conducted in Jiangsu Province, China (Figure 1A). It covers an area of 107 200 km^2 and has 13 prefecture-level cities. In 2022, the gross domestic product (GDP) of Jiangsu Province reached 12 287.56 billion yuan, with a permanent resident population of 85 million.[21] Public health emergencies are frequent in Jiangsu due to its large and densely distributed population.[22] Historically, malaria was highly prevalent in Jiangsu Province.[23] In Jiangsu Province, *Anopheles sinensis* and *Anopheles anthropophagus* are the dominant mosquito vectors, and the climate and environment are suitable for the breeding of *Anopheles* mosquitoes from May to October, coinciding with the malaria transmission season.[23] Jiangsu Province reported its last indigenous malaria case in 2011 and interrupted local malaria transmission by 2012. In 2018, a provincial-level malaria elimination assessment was conducted in Jiangsu Province, and the province was certified as malaria-free.[24]

Study design and data source

We conducted a retrospective analysis of patients with confirmed imported malaria from 1 June 2012 to 31 December 2019 using routine surveillance data from the China Information System for Disease Control and Prevention, which is a real-time, web-based infectious disease surveillance and response system.

Definition of imported malaria

In China, the following criteria for imported malaria must be met: (i) with a laboratory diagnosis of malaria; (ii) a travel history to malaria-endemic areas outside China during the malaria transmission season; (iii) malaria onset <1 month after returning to China during the local transmission season.[25] If all of the above criteria are not met, the case is classified as local. When there is a need, the case classification is determined during regular routine meetings of provincial or national experts.[15]

Missing data

The quantity of missing data was first assessed and then handled. If <5% of cases are were missing per variable, a complete case analysis was appropriate.[26,27] A variable that was missing in >5% of cases was handled through multiple imputation before building the ML models.[28] While there is no upper limit, in this study, we considered it reasonable to impute 10–30% of missing values per variable.[29] To ensure that the imputation was performed adequately, we verified the process by comparing the distribution of the imputed data with the observed data. Variables with more than 30% missing data were dropped.

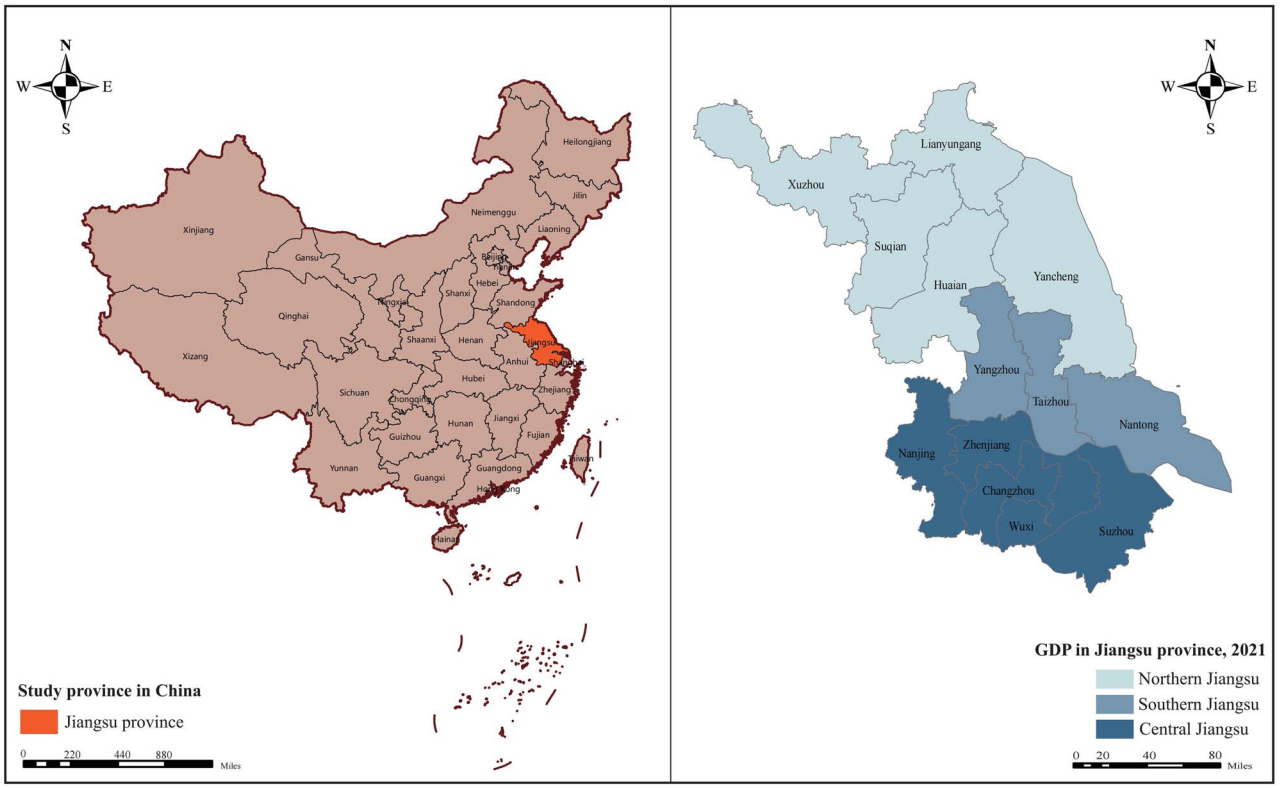

Figure 1 Location of Jiangsu province in eastern China (A) and the classification of the provinces into three categories according to their economic development (B)

Measures

Delayed care-seeking. The timing of seeking healthcare among patients with imported malaria was the primary outcome. WHO has emphasized that early diagnosis and prompt treatment for malaria should occur within 24 h of the onset of symptoms to decrease the risk of severe complications and onwards transmission. Thus, a delay in care-seeking was defined as a period of >24 h between the onset of symptoms and treatment being sought at a malaria clinic or public hospital. Moreover, in this study, considering logistical realities in China, we further assessed the risk of care-seeking >3 days after symptom onset in a malaria clinic or public hospital after the onset of symptoms.

Variables. All potential variables are selected a priori based on epidemiological/clinical importance and accessibility. Detailed features extracted from every malaria patient were carefully reviewed and verified. The variables include the patient's age, sex, country visited, purpose of the visits, malaria infection history (a certain proportion of imported malaria patients were migrant workers and thus may have regularly visited malaria-endemic regions and had a malaria infection history), date of return to China, date of symptom onset, date of first visit to a medical facility, level of the medical facilities at which medical attention was sought, species of pathogen and the GDP of the destination city in 2021 (Figure 1B).[30]

Statistical analysis and nomogram model development

Continuous variables with a normal distribution are presented as the mean ± standard deviation, and categorical variables are expressed as percentages with corresponding 95% confidence intervals (CIs). Statistical significance was set at $P < 0.05$. An ML regression analysis based on the results of the univariate analyses was performed to calculate the odds ratios (ORs) and 95% CIs of the independent variables. The multicollinearity of the independent variables was checked via the variance inflation factor statistic. Variables included in the final multivariable models were selected according to their physiological relevance and statistical significance in univariate analysis using a P-value threshold of 0.05. All statistical tests were two-sided, and results with P values < 0.05 were considered statistically significant. The above statistical tests were performed with R version 4.2.0. Based on the multivariable analysis of the training set, a predictive nomogram model was plotted.

Machine learning model development and validation

The applied computational architecture included the following four different algorithms: MLP, LSVM, RF, LR and Bayesian models. We randomly assigned 1545 patients (70%) to a training cohort and 710 patients (30%) to a test cohort. The models were established by SPSS 28.0 software, R and Modeller 18.0.

MLP is a popular machine learning algorithm that can automatically find hidden patterns and is formulated as a hierarchical stack of ensemble linear classifiers, each with nonlinear activation. MLP was based on the backpropagation of the cross-entropy classification error on training samples, which iteratively updated the linear weights of the linear classifier so that classification error was reduced.[31,32] In this case, three main layers were constructed. The input layer consisted of routinely available variables. The activation function of each neuron was set as a softmax function.[33] The optimization algorithm of the MLP model was a standard conjugate gradient. Based on the training dataset, the performance of the model was evaluated by 10-fold cross-validation, and the optimal number of hidden layer units and the maximum number of iterations of the model were determined. To avoid overfitting, the coefficient of regularization was set as 0.001. Then, we trained the final MLP model based on the entire training dataset using the best model parameters obtained in the evaluation process. The LSVM, RF and Bayesian models were performed by Modeller 18.0. The regularization type of LSVM was L2 regularization (which is classically used to reduce overfitting).[34] RF fit 100 classification trees. The parameters of the tree model were set as follows: a maximum tree depth of 10, a maximum number of nodes of 10 000 and a minimum child node size of 5.

Further validation of the models

In the test set (the remaining 30% of the sample), we computed the prediction performance of each model that was derived above. For prediction performance, we computed (i) the area under the receiver operating characteristic curve (AUC), which plots the sensitivity (i.e. the true-positive rate) against 1 − the specificity (i.e. the false-positive rate). A model with an AUC > 0.8 is usually considered to have good discrimination, while anything <0.6 is considered poor.[35] (ii) Confusion matrix results (i.e. sensitivity, specificity, Youden's index) and (iii) calibration curves were also determined. To compare the receiver operating characteristic curves between models, the Z test was used. All comparisons were two-sided, with statistical significance defined as $P < 0.05$. Analyses were performed with R version 4.2.0.

Ethical aspects

Data were anonymized prior to the statistical analysis. This study was registered as a nationally funded research project with the aim of improving the case management of patients with imported malaria (registration no. 71904165).

Results

Characteristics of the study population

The detailed demographic characteristics of the 2255 Chinese patients with imported malaria from 2012 to 2019 are summarized in Table 1. Importantly, a total of 96.8% (2171/2255) of the patients were migrant workers, and nearly all were middle-aged males. Sub-Saharan Africa (SSA) was the most frequent region of origin (78.4%, 1768/2255). Regarding the timing of symptom onset, 41.4% (933/2255) of the patients developed symptoms within 1 week after entry, and 40.7% (918/2255) of the patients developed symptoms between 1 week and 1 month after entry. Very few (1.2%, 27/2255) patients developed symptoms before entry to China. Medical attention was most frequently sought in county-level healthcare institutions first (50.1%, 1130/2255). Out of the 2255 patients with imported malaria, only ∼28.2% (636/2255) sought healthcare within 24 h after symptom onset. Moreover, a quarter of the patients (25.6%, 577/2255) accessed healthcare 3 days after the onset of the symptoms, clearly representing delayed care-seeking.

Predictive factors for delayed care-seeking

An ML regression analysis showed that three factors were independent predictors of delayed care-seeking behaviour in patients with imported malaria: the GDP of the reported area, the timing of symptom onset (developed before or after entry into China) and the level of the healthcare facility at which health care was initially sought. Detailed results are as follows: a time to symptom onset within 1 week after entry ($P = 0.003$, OR = 0.183, 95% CI: 0.060∼0.563), a time to symptom onset between 1 week and 1 month after entry ($P = 0.001$, OR = 0.122, 95% CI: 0.040∼0.375), a time to symptom onset 1 month after entry ($P = 0.016$, OR = 0.240, 95% CI: 0.075∼0.763), a GDP of the destination city in the second category ($P = 0.320$, OR = 0.868, 95% CI: 0.656∼1.148), a GDP of the destination city in the third category ($P = 0.007$, OR = 0.634, 95% CI: 0.457∼0.881), and first seeking medical attention in township healthcare institutions ($P = 0.019$, OR = 2.401 95% CI: 1.155∼4.991), county healthcare institutions ($P < 0.001$, OR = 3.833, 95% CI: 2.096∼7.006), municipal healthcare institutions ($P < 0.001$, OR = 4.103, 95% CI: 2.207∼7.627) and provincial healthcare institutions ($P < 0.001$, OR = 5.702, 95% CI: 2.512∼12.945) (Table 2).

Risk prediction nomogram development and validation

The logistic regression model was constructed based on the above factors (Table 2). A nomogram was established based on the logistic regression model (Figure 2). For each patient, higher total number of points indicated a higher risk of delayed care-seeking. For example, if a returning migrant worker with malaria was reported in Suzhou (a city with a GDP in the first category), had a symptom onset within 1 week after entry and initially sought care in a township-level health facility, then the corresponding scores of this imported malaria patient were ∼25, 22 and 41, respectively. The patient's total score is ∼88, indicating an estimated delayed care-seeking risk of 25%. The calibration curves of the nomogram showed high consistency between the predicted and observed probabilities of care-seeking delays in both the training and validation sets (Figure S1 available as Supplementary data at *JTM* online).

ML-based models to predict care-seeking among patients with imported malaria

Regarding the prediction of care-seeking within 24 h and 3 days after symptom onset among patients with imported malaria, the discriminatory abilities of all five models (the MLP, LSVM, RF, LR and Bayesian models) are summarized in Table S1 available

Table 1 Basic characteristics and behaviour among patients with imported malaria in Jiangsu Province, from June 2012 to December 2019

Characteristics ($n = 2255$)	Number (%)
Sex	
Male	2194 (97.6)
Female	61 (2.7)
Age (years)	
Median (IQR)	44 (36–49)
Region of travel	
Sub-Saharan Africa (SSA)	1768 (78.4)
Non-SSA countries in Africa	415 (18.5)
Others	72 (3.2)
Economic development of the destination city	
Southern Jiangsu	698 (31.0)
Central Jiangsu	960 (42.5)
Northern Jiangsu	597 (26.5)
Timing of symptom onset	
Prior to entry	27 (1.2)
Within 1 week after entry	933 (41.4)
From a week to 1 month after entry	918 (40.7)
After 1 month	377 (16.7)
Duration from symptom onset to healthcare seeking	
Within 24 h	636 (28.2)
From 24 to 48 h	641 (28.4)
From 48 to 72 h	401 (17.8)
Longer than 3 days	577 (25.6)
Symptoms	
Fever only	637 (28.3)
Fever together with other symptoms	1578 (70.0)
Other symptoms without fever	34 (1.5)
Asymptomatic	4 (0.2)
Returning season	
From November to January	636 (28.3)
From February to March	462 (20.5)
From April to June	607 (26.9)
From July to October	546 (24.3)
The interval between last infection and current infection	
No history of infection	740 (33.0)
0–1 month	227 (10.1)
2–3 months	574 (25.6)
4–6 months	288 (12.8)
More than half a year	414 (18.5)
Country of travelling	
Sub-Saharan Africa (SSA)	1768 (78.4)
Non-SSA countries in Africa	415 (18.4)
Others	72 (3.2)
The level of the healthcare facility at which healthcare was initially sought[a]	
Village clinics and private clinics	191 (8.5)
Township healthcare institutions	198 (8.8)
County healthcare institutions	1130 (50.1)
Municipal healthcare institutions	654 (29.0)
Provincial healthcare institution	82 (3.6)

[a]Township healthcare institutions include Township CDCs and hospitals; county healthcare institutions include County CDCs and hospitals; municipal healthcare institutions include City CDCs and hospitals.

as Supplementary data at *JTM* online. In both scenarios, the MLP model demonstrated a significantly higher AUC ($P < 0.001$).

The variable importance ranking in the MLP model is shown in Figure 3. Regarding the prediction of delayed care-seeking at 3 days after symptom onset, the time of symptom onset, the level of the healthcare facility at which care was initially sought, country of origin, symptoms and return time were identified as the most significant factors. Regarding the prediction of delayed care-seeking 24 h after symptom onset, the top five influencing factors were the level of the healthcare facility at which care was initially sought, time of symptom onset, time interval between the last and current infection, return time and initial symptoms.

Table 2 Multivariate analysis of risk factors for delayed care-seeking among international migrant workers with imported malaria in China

Variable	β	Wald test	Odds ratio (95% CI)	*P* value
Intercept	−0.788	2.414		
The GDP of the destination city				
First	Reference			
Second	−0.142	0.990	0.868 (0.656–1.148)	0.320
Third	−0.455	7.402	0.634 (0.457–0.881)	0.007
Timing of symptom onset				
Pre-entry	Reference			
Within 1 week after entry	−1.698	8.773	0.183 (0.060–0.563)	0.003
From a week to 1 month after entry	−2.105	13.449	0.122 (0.040–0.375)	<0.001
After 1 month	−1.428	5.852	0.240 (0.075–0.763)	0.016
The level of the healthcare facility at which healthcare was initially sought				
Village clinics and private clinics	Reference			
Township healthcare institutions	0.876	5.508	2.401 (1.155–4.991)	0.019
County healthcare institutions	1.344	19.051	3.833 (2.096–7.006)	<0.001
Municipal healthcare institutions	1.412	19.912	4.103 (2.207–7.627)	<0.001
Provincial healthcare institution	1.741	17.318	5.702 (2.512–12.945)	<0.001

Note: β, regression coefficient; OR, odds ratio; CI, confidence interval. According to economic development, reported areas in southern Jiangsu, northern Jiangsu and central Jiangsu were categorized into the first, second and third categories, respectively. Southern Jiangsu had a GDP of 6.7 trillion yuan, northern Jiangsu had a GDP of 2.7 trillion yuan and central Jiangsu had a GDP of 2.4 trillion yuan in 2021. *P* was set at <0.05 for the multivariable results. Variables were excluded based on univariate analysis: sex ($P = 0.191$), age ($P = 0.804$), purpose of the visit ($P = 0.056$), complications ($P = 0.117$), species of pathogen ($P = 0.162$), severity of malaria ($P = 0.81$) and duration of being abroad ($P = 0.956$). Variables were further excluded based on multivariate analysis ($P < 0.05$): country of travel ($P = 0.264$), malaria infection history ($P = 0.886$), returning season ($P = 0.16$), and the interval between last infection and current infection ($P = 0.224$).

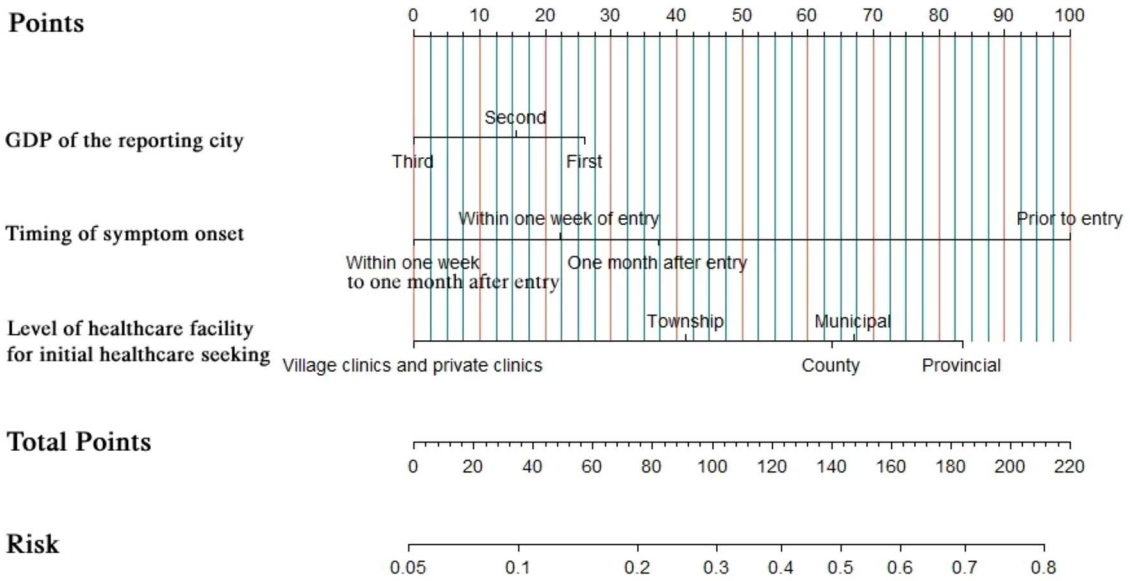

Figure 2 A nomogram tool predicts the risk of care-seeking delay (3 days after symptom onset) of imported malaria

Discussion

For formerly malaria-endemic areas to maintain a malaria-free status, the establishment of a well-functioning surveillance and response system for rapid diagnosis and treatment is essential.[9] Moreover, it is of overall importance that patients themselves promptly seek healthcare after symptom onset.[15] Therefore, here, we present an analysis of migrant workers with imported malaria between 2011 and 2019 in Jiangsu Province, China. Moreover, our study is the first to develop a nomogram model to predict the risk of delayed care-seeking among patients with imported malaria. Our study revealed that the GDP of the destination area, the timing of symptom onset and the level of the healthcare facility at which healthcare was initially sought were predictors of delayed care-seeking among migrant workers with imported malaria. The nomogram could be used as a practical tool for health workers and policymakers seeking to develop targeted interventions to improve access and the provision of post-travel healthcare for international travellers, particularly international migrant workers.

In addition to confirming that the majority of patients with imported malaria in China were migrant workers and their tendency towards delayed care-seeking behaviour after symptom

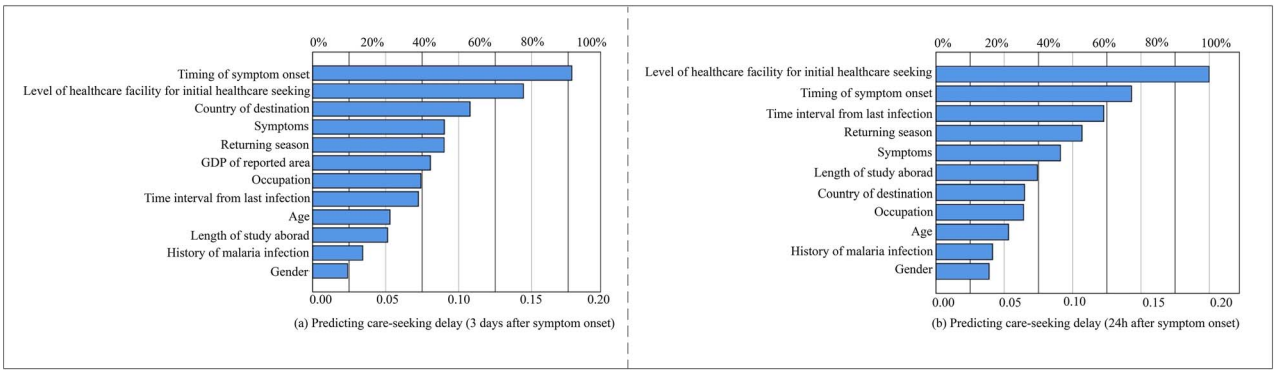

Figure 3 Variable importance of predictors in the MLP. The variable importance is scaled measure to have a maximum value of 100%

onset,[36] we have further revealed some new epidemiological characteristics of imported malaria patients in China. Nearly two-thirds of the patients had a history of imported malaria infection, which means that a certain number of imported malaria patients are not unfamiliar with malaria. This could be explained by the fact that international migrant labourers with malaria in China are either regularly visiting countries in SSA or have much prolonged stays.[10,11] Thus, health agencies should carefully consider this characteristic in designing and improving pre-travel and post-travel health education programmes for these groups. Traditional health education programmes, which are usually designed for travellers visiting friends or relatives and mainly focus on improving malaria knowledge (e.g. symptoms), may not be enough, as many migrant workers have experience with malaria treatment and even bring medication from African countries when returning to China. In particular, considering the rising threat posed by counterfeit anti-malaria drugs,[37] it is significant to carry out awareness campaigns among the migrant workers regarding the proper use of antimalarials and discourage the practice of self-medication.

Our study demonstrated that many malaria patients developed initial symptoms within 1 month after entry (82.1%). It was indicated that enrolling village doctors to function as a reminder for migrant workers returning from malaria-endemic countries to seek healthcare promptly is crucial, as village doctors usually live in villages, know villagers well and visit households frequently. Moreover, although the majority of the patients with imported malaria developed symptoms within 1 month after entry, it is also important to note that nearly 20% of the patients developed malaria symptoms >1 month after entry. Considering the incubation features of different species of *Plasmodium*, individuals who developed symptoms 1 month after infection were more likely to be infected with *Plasmodium ovale* and *Plasmodium malariae*.[38] Moreover, the severity of the symptoms of these two types is rather moderate compared with *Plasmodium falciparum*,[39] which may be more likely to be overlooked and cause delayed care-seeking and diagnosis. Therefore, general health service providers should maintain vigilance regarding fever patients with a travel history some time ago.[40]

Our study demonstrated that the development of symptoms before entry into China was more likely to delay care-seeking than the development of symptoms after entry into China; this may be explained by the fact that patients may already seek healthcare during their stay abroad. Considering that the majority of patients with imported malaria in China were returning from SSA, they might have purchased anti-malaria medication from local private chemical shops in the workplace or received medication from export labour companies.[41,42] However, it should be noted that in these cases, the quality of the medication and the standard of treatment may not be guaranteed.[43,44] Thus, malaria-related knowledge should be provided to international migrant workers to increase their awareness of malaria prevention.[45] Export labour companies/agencies should be largely involved and that they should be trained in providing qualified healthcare to migrant workers during their work abroad, not only in healthcare for malaria but also for other infectious diseases.

Consistent with previous findings, initially seeking healthcare in facilities with a higher administrative level was significantly associated with delayed care-seeking among imported malaria patients. This could be explained by the fact that once patients plan to seek healthcare in village clinics or private clinics, they are more likely to access these grassroots health facilities (e.g. village clinics) rapidly and quickly than those who seek healthcare at provincial or city-level health facilities.[15] A previous study demonstrated that a distance >3 km from the health facility was found to be the main determinant of care-seeking delays among malaria patients in Ethiopia.[46] However, village or township health facilities generally have a limited diagnostic capacity for malaria, and thus, patients may be misdiagnosed in rural regions.[47,48] Health practitioners at superior Centers for Disease Control and Prevention (CDCs) and hospitals usually have a higher education background and better capacity in performing and interpreting blood smears.[48] Therefore, improving access to higher-level healthcare facilities and improving the medical capacity of primary health facilities in China are crucial for early malaria diagnosis and treatment.

Interestingly, the third independent predictor of delayed care-seeking demonstrated here was case reporting in more economically developed regions (with a higher GDP level). Increasing incomes are generally associated with improvements in health.[49] However, on the other hand, increasing incomes can also lead to unexpected increases in the number of illnesses and diseases, and there may be an increase in the demand for health resources.[49] Moreover, health resources are more likely to be unequally distributed in more economically developed cities with larger

populations. For example, Guangdong Province, a leading GDP province in China, has 2.5 doctors per 1000 people, which is less than the average level across all of China (3.56 doctors per 1000 people).[50,51] Moreover, those international migrant labourers generally live in rural areas even in large cities where they usually still face limited medical resources.[52] Therefore, it is important to improve healthcare access and equality even in economically developed cities, particularly among individuals who are poor and have a low socioeconomic status.

Although the MLP-based model demonstrated better performance, the ML-based models generally did not show a significant improvement in predicting the risk of care-seeking delays among migrant workers with imported malaria compared with the logistic regression models. In the MLP model, the timing of symptom onset, the level of the healthcare facility at which healthcare was initially sought and the major symptoms were identified as important factors associated with delayed care-seeking among international migrant workers with imported malaria. The findings are somewhat consistent with the findings from the regression analysis and nomogram prediction tool. Therefore, the practical scoring system of the nomogram provided public health practitioners with an accurate and effective tool for the early prediction and improvement of delayed care-seeking behaviour after their returning to China.

Policy implications

The imported malaria patients in China are usually low social class labourers who often work in conditions that place them at increased risk of malaria (e.g. mining, construction sites, forest work), are not well protected at night due to poor accommodations, have a low education level and thus lack awareness of malaria risks, have no specific immunity and often have limited access to health services.[53] Therefore, this study developed a nomogram tool to evaluate the risk of care-seeking delays, which could be used for further development of interventions to improve the healthcare-seeking behaviour of migrant workers with imported infectious diseases, particularly imported malaria. By developing this tool, importantly, labour companies or agencies, which are mainly responsible for sending migrant workers abroad, should engage in the provision of pre-travel health education, reminding workers of the importance of early and proper post-travel care-seeking.

Study limitations

There are several limitations to our study. First, the time of malaria onset and initial care-seeking were recorded in the surveillance system as the number of days and not as the exact number of hours, which would have been more accurate. Second, although a careful epidemiological investigation for each imported malaria patient was performed through the 1–3–7 surveillance and response working scheme and the data quality was rather good, some potentially meaningful predictors, such as the perceived quality of services, were not assessed due to lack of data. Moreover, although the overall large sample size of this study ensured the reliability of the analysis, there is still room for improvement regarding the completeness of the surveillance data. Finally, the patients from the training and validation cohorts can only be considered representative of the population of southeast China; therefore, we will seek to carry out an external validation assessment in a multicentre study.

Conclusions

Our study found that the timing of symptom onset, the GDP of the destination city and the level of the healthcare facility at which healthcare was initially sought were predictors of delayed care-seeking among migrant workers with imported malaria. Based on these predictors, we built an easy-to-use nomogram for the early prediction of delayed care-seeking behaviour among migrant workers, and our internal validation confirmed that the performance of the model was good. This visual model provides public health practitioners with a simple and intuitive tool for the early detection and identification of delayed care-seeking risk among migrant workers with malaria, which may be of significance in improving healthcare access among imported malaria patients, reducing the risk of severe malaria, preventing malaria reintroduction and therefore sustaining malaria elimination success.

Supplementary data

Supplementary data are available at *JTM* online

Funding

This work was supported by the National Natural Science Foundation of China (Grant no. 72374178); National Natural Science Foundation of China (Grant no. 71904165); the Open Project Program of Jiangsu Key Laboratory of Zoonosis (Grant no. R2208); the Open Project Program of International Research Laboratory of Prevention and Control of Important Animal Infectious Diseases and Zoonotic Diseases of Jiangsu Higher Education Institutions [01]; the Open Project Program of National Health Commission Key Laboratory of Parasitic Disease Control and Prevention Jiangsu Provincial Key Laboratory on Parasite and Vector Control Technology (Grant no. wk023-007), and the Jiangsu Provincial Health Commission (H2023004, and X202315).

Author contributions

Jiyue Gu (Data curation [equal], Writing—original draft [equal]), Yuanyuan Cao (Data curation [equal], Writing—original draft [equal]), Liying Chai (Writing—original draft [equal]), Enyu Xu (Formal analysis [equal], Software [equal], Visualization [equal]), Kaixuan Liu (Formal analysis [equal], Software [equal], Visualization [equal]), Zeyin Chong (Data curation [equal]), Yuying Zhang (Formal analysis [equal], Software [equal], Visualization [equal]), Dandan Zou (Formal analysis [equal], Software [equal], Visualization [equal]), Yuhui Xu (Investigation [supporting], Validation [equal], Visualization [equal]), Jian Wang (Resources [equal], Supervision [equal], Validation [equal]), Olaf Müller (Software [equal], Visualization [equal], Writing—review & editing [equal]), Jun Cao (Writing—review & editing [equal]), Guoding Zhu (Conceptualization [equal], Writing—review & editing [equal]), and Guangyu Lu (Conceptualization [equal], Writing—review & editing [equal])

Conflict of interest: None declared.

Data availability

The data generated and analysed during this study are not publicly available due to risk of deductive disclosure. Access may be requested from Prof. Guangyu Lu (guangyu.lu@yzu.edu.cn) and Prof. Guoding Zhu (jipdzhu@hotmail.com), and will be granted subject to approval and a data sharing contract.

References

1. World Health Organization. *World Malaria Report* 2021. https://apps.who.int/iris/rest/bitstreams/1398397/retrieve (13 June 2023, date last accessed).
2. Dhiman S. Are malaria elimination efforts on right track? An analysis of gains achieved and challenges ahead. *Infect Dis Poverty* 2019; **8**:14.
3. Rogerson SJ, Beeson JG, Laman M *et al.* Identifying and combating the impacts of COVID-19 on malaria. *BMC Med* 2020; **18**:239.
4. Liu Q, Jing W, Kang L, Liu J, Liu M. Trends of the global, regional and national incidence of malaria in 204 countries from 1990 to 2019 and implications for malaria prevention. *J Travel Med* 2021; **28**:taab046.
5. Müller O, Lu G, Jahn A, Razum O. Malaria eradication. *Lancet* 2020; **395**:e68.
6. National Health Commission of the People's Republic of China. *Action Plan of China Malaria Elimination (2010–2020)*. Published in 19 May 2021. http://www.gov.cn/zwgk/2010-05/26/content_1614176.htm (13 June 2023, date last accessed).
7. Zhou XN. China declared malaria-free: a milestone in the world malaria eradication and Chinese public health. *Infect Dis Poverty* 2021; **10**:98.
8. Cao J, Newby G, Cotter C *et al.* Achieving malaria elimination in China. *Lancet Public Health* 2021; **6**:e871–2.
9. Nasir SMI, Amarasekara S, Wickremasinghe R, Fernando D, Udagama P. Prevention of re-establishment of malaria: historical perspective and future prospects. *Malar J* 2020; **19**:452.
10. Lu G, Zhou S, Horstick O, Wang X, Liu Y, Müller O. Malaria outbreaks in China (1990-2013): a systematic review. *Malar J* 2014; **13**:269.
11. Jelinek T. Imported falciparum malaria in Europe: 2007 data from TropNetEurop. *Euro Surveill* 2008; **13**:18895.
12. Smith DL, Cohen JM, Chiyaka C *et al.* A sticky situation: the unexpected stability of malaria elimination. *Philos Trans R Soc Lond B Biol Sci* 2013; **368**:20120145.
13. Hänscheid T. Current strategies to avoid misdiagnosis of malaria. *Clin Microbiol Infect* 2003; **9**:497–504.
14. Checkley AM, Smith A, Smith V *et al.* Risk factors for mortality from imported falciparum malaria in the United Kingdom over 20 years: an observational study. *BMJ* 2012; **344**:e2116.
15. Lu G, Cao Y, Chen Q, Zhu G, Müller O, Cao J. Care-seeking delay of imported malaria to China: implications for improving post-travel healthcare for migrant workers. *J Travel Med* 2022; **29**:taab156.
16. Bastaki H, Carter J, Marston L, Cassell J, Rait G. Time delays in the diagnosis and treatment of malaria in non-endemic countries: a systematic review. *Travel Med Infect Dis* 2018; **21**:21–7.
17. Sonkong K, Chaiklieng S, Neave P, Suggaravetsiri P. Factors affecting delay in seeking treatment among malaria patients along Thailand-Myanmar border in Tak Province, Thailand. *Malar J* 2015; **14**:3.
18. Zhang T, Wang D, Qian Y *et al.* Profile and determinants of delayed care-seeking and diagnosis among patients with imported malaria: a retrospective study in China, 2014-2021. *Infect Dis Poverty* 2022; **11**:125.
19. Flateau C, Picque M, Cornaglia C *et al.* Factors associated with delay in seeking healthcare for imported malaria: a retrospective study in a French hospital. *J Travel Med* 2023; **30**:taad023.
20. Keys HM, Noland GS, De Rochars MB *et al.* Prevalence of malaria and lymphatic filariasis in bateyes of the Dominican Republic. *Infect Dis Poverty* 2019; **8**:39.
21. The People's Government of Jiangsu Province. *A Snapshot of the Province's Economic Performance from January to December 2022*. Published 21 January 2023. http://www.jiangsu.gov.cn/art/2023/1/21/art_34151_10732838.html (20 June 2023, date last accessed).
22. The People's Government of Jiangsu Province. *Statistical Bulletin on National Economic and Social Development of Jiangsu Province in 2022*. Published 03 March 2023. http://tj.jiangsu.gov.cn/art/2023/3/3/art_85275_10787011.html (20 July 2023, date last accessed).
23. Zhu G, Zhou H, Li J *et al.* The colonization of pyrethroid resistant strain from wild Anopheles sinensis, the major Asian malaria vector. *Parasit Vectors* 2014; **7**:582.
24. Cao Y, Lu G, Cotter C *et al.* Improving the surveillance and response system to achieve and maintain malaria elimination: a retrospective analysis in Jiangsu Province, China. *Infect Dis Poverty* 2022; **11**:20.
25. Feng J, Yan H, Feng XY *et al.* Imported malaria in China, 2012. *Emerg Infect Dis* 2014; **20**:1778–80.
26. Haukoos JS, Newgard CD. Advanced Statistics: Missing Data in Clinical Research—Part 1: an introduction and conceptual framework. *Acad Emerg Med* 2007; **14**:662–8.
27. Hughes RA, Heron J, Sterne JAC, Tilling K. Accounting for missing data in statistical analyses: multiple imputation is not always the answer. *Int J Epidemiol* 2019; **48**:1294–304.
28. Hong S, Lynn HS. Accuracy of random-forest-based imputation of missing data in the presence of non-normality, non-linearity, and interaction. *BMC Med Res Methodol* 2020; **20**:199.
29. Gravesteijn BY, Sewalt CA, Venema E *et al.* Missing data in prediction research: a five-step approach for multiple imputation, illustrated in the CENTER-TBI study. *J Neurotrauma* 2021; **38**:1842–57.
30. Statistical Bureau of Jiangsu Province. *Jiangsu Statistical Year Book*, 2022. http://stats.jiangsu.gov.cn/2020/nj20/nj0212.htm (20 July 2023, date last accessed).
31. Kalagotla SK, Gangashetty SV, Giridhar K. A novel stacking technique for prediction of diabetes. *Comput Biol Med* 2021; **135**:104554.
32. Bizjak Ž, Pernuš F, Špiclin Ž. Deep shape features for predicting future intracranial aneurysm growth. *Front Physiol* 2021; **12**:644349.
33. Kriegeskorte N, Golan T. Neural network models and deep learning. *Curr Biol* 2019; **29**:R231–r236.
34. Samper-González J, Burgos N, Bottani S *et al.* Reproducible evaluation of classification methods in Alzheimer's disease: framework and application to MRI and PET data. *Neuroimage* 2018; **183**:504–21.
35. Swets JA. Measuring the accuracy of diagnostic systems. *Science* 1988; **240**:1285–93.
36. Yu T, Fu Y, Kong X, Liu X, Yan G, Wang Y. Epidemiological characteristics of imported malaria in Shandong Province, China, from 2012 to 2017. *Sci Rep* 2020; **10**:7568.
37. Karunamoorthi K. The counterfeit anti-malarial is a crime against humanity: a systematic review of the scientific evidence. *Malar J* 2014; **13**:209.
38. Collins WE, Jeffery GM. Plasmodium ovale: parasite and disease. *Clin Microbiol Rev* 2005; **18**:570–81.
39. Garcia LS. Malaria. *Clin Lab Med* 2010; **30**:93–129.

40. World Health Organization. *The E-2020 Initiative of 21 Malaria-Eliminating Countries: 2019 Progress Report*. Published 18 June 2019. https://www.who.int/publications/i/item/WHO-CDS-GMP-2019.07 (20 June 2023, date last accessed).
41. Ansah EK, Gyapong M, Narh-Bana S, Bart-Plange C, Whitty CJM. Factors influencing choice of care-seeking for acute fever comparing private chemical shops with health centres and hospitals in Ghana: a study using case-control methodology. *Malar J* 2016; **15**:290.
42. Mpimbaza A, Katahoire A, Rosenthal PJ, Karamagi C, Ndeezi G. Caregiver responses and association with delayed care-seeking in children with uncomplicated and severe malaria. *Malar J* 2018; **17**:476.
43. Brower V. Counterfeit and substandard malaria drugs in Africa. *Lancet Infect Dis* 2017; **17**:1026–7.
44. Arora T, Sharma S. Global scenario of counterfeit antimalarials: a potential threat. *J Vector Borne Dis* 2019; **56**:288–94.
45. Lu G, Cao Y, Zhang D *et al.* Implementation and challenges to preventing the re-establishment of malaria in China in the COVID-19 era. *Global Health* 2022; **18**:64.
46. Regassa H, Taffere GR, Gebregergs GB. Delay in malaria diagnosis and treatment and its determinants among rural communities of the Oromia special zone, Ethiopia: facility-based cross-sectional study. *J Public Health* 2018; **26**:339–44.
47. Podgorelec V, Kokol P, Stiglic B, Rozman I. Decision trees: an overview and their use in medicine. *J Med Syst* 2002; **26**:445–63.
48. Ding G, Zhu G, Cao C *et al.* The challenge of maintaining microscopist capacity at basic levels for malaria elimination in Jiangsu Province, China. *BMC Public Health* 2018; **18**:489.
49. Lange S, Vollmer S. The effect of economic development on population health: a review of the empirical evidence. *Br Med Bull* 2017; **121**:47–60.
50. The Global Economy. *Doctors per 1,000 People—Country Rankings*. https://www.theglobaleconomy.com/rankings/doctors_per_1000_people/ (20 December 2023, date last accessed).
51. Ministry of Health in Guangdong Province. *Ministry of Health in Guangdong Province*. Published 12 September 2023. http://szyyj.gd.gov.cn/zwgk/tjxx/content/post_4252846.html (20 December 2023, date last accessed).
52. Sim F, Mackie P. Well-being of the migrant workforce: who cares? *Public Health* 2018; **160**:A1–a2.
53. Liu Y, Hsiang MS, Zhou H *et al.* Malaria in overseas labourers returning to China: an analysis of imported malaria in Jiangsu Province, 2001-2011. *Malar J* 2014; **13**:29.