

# Analysis of Epidemiological Changes and Elimination Effects for Malaria in Handan City, China

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## Research

**Keywords:** Malaria, Imported malaria, Surveillance, Evaluation, Elimination

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**Analysis of epidemiological changes and elimination effects for malaria in Handan city, China**

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23 **Abstract**

24 **Background:** The elimination of malaria requires high-quality surveillance data in order  
25 to detect and respond quickly to individual cases. In the 1960s and 1970s, Handan city  
26 experienced widespread malaria outbreaks, which was in line with the provincial and  
27 national epidemic patterns.

28 **Methods:** Case-level data for the period 2011-2018 were extracted from China's  
29 National Infectious Diseases Information system and the rest cases were recorded  
30 municipal surveillance system from 1956-2010.

31 **Results:** The incidence, accuracy and timeliness of case diagnosis, reporting and  
32 investigation in malaria were evaluated at elimination stage (2011-2018) in Handan city,  
33 China. From 2011 to 2018, 81 malaria cases were reported in Handan city, all of which  
34 were imported from abroad. The annual average incidence decreased to 0.11/100 000  
35 in the elimination stage, while all malaria cases were male. Since the initiation of the  
36 National Malaria Elimination Programme in 2010, malaria cases were consistent with  
37 the increase in overseas export channels and personnel of labor services.

38 **Conclusions:** The case-based malaria surveillance system in Handan worked well at  
39 the malaria elimination stage. This ensured that malaria cases could be diagnosed,  
40 reported and timely investigated at local level.

41 **Keywords:** Malaria, Imported malaria, Surveillance, Evaluation, Elimination

42

43 **Background**

44 Malaria is considered one of the most significant health problems for humans with a

45 substantial disease burden in tropical areas. Malaria results from a vector borne  
46 plasmodial infection with single-celled parasites belonging to the *Plasmodium genus*  
47 and transmitted via the bites of the female *Anopheles mosquito*[1]. In 2017, there were  
48 approximately 219 million cases of malaria responsible for about 435000 deaths, the  
49 majority on the African. Outstanding progress has been made in malaria control over  
50 the past decade[2-4]. More and more countries are progressing to elimination. As of  
51 December 2017, of the 106 countries with sustained transmission of malaria in 2000,  
52 19 countries attained zero indigenous cases for 3 years or more; 16 of these countries  
53 that eliminated malaria between 2007 and 2017. To achieve the goal of eliminating  
54 malaria, a sustainable and well-functioning malaria monitoring system is considered as  
55 a key measure[5]. World Health Organization (WHO) launched a new initiative on  
56 global malaria programme 3T, Test, Treatment and Track in 2012, which depends on  
57 the provision of timely and accurate monitoring data to monitor performance and  
58 identify threats to malaria control and elimination[6].

59 In the past, especially in the last 30-40 years after the founding of the People's  
60 Republic of China, China has suffered from severe malaria epidemics[7]. From 1949  
61 to 2020, the transmission of the malaria can be primarily divided into four phases:  
62 transmission; outbreak and pandemic transmission; decline with sporadic distribution;  
63 and the elimination phase[8]. A national malaria elimination programme (NMEP) was  
64 launched in China in 2010, which supports to achieve zero indigenous case of malaria  
65 within the 2020 timeline[9]. The elimination phase is different from the control phase,  
66 and needs to monitor and respond to each malaria infection, and to eventually stop local

67 malaria transmission. China has developed a case-based malaria surveillance system to  
68 gather information needed for diagnosis and investigation, and to promote a rapid  
69 response to individual cases[10, 11]. In order to eliminate malaria, the strengths and  
70 limitations of the program must be understood by quantitatively evaluating the  
71 performance and efficiency of NMEP[12, 13].

72 According to the report from WHO in 2018, there were 20 million fewer cases in  
73 2017 than in 2010 globally. At the same time, increasing labour service and travel to  
74 malaria-endemic areas in recent decades has resulted in a steady increase in the number  
75 of imported cases in non-endemic countries[14]. Malaria poses a serious health hazard  
76 to travelers to local areas. Imported malaria is an infection acquired abroad and brought  
77 into the regional territory[15]. Cases imported-malaria into non-endemic countries tend  
78 to lead to delayed diagnosis, expensive treatment and, sometimes, secondary local  
79 transmission[16]. During 2017-2019, China had achieved interruption of indigenous  
80 malaria transmission. Still, malaria is the imported disease with the highest number of  
81 notifications in China, between 2500 and 10000 malaria cases are imported into China  
82 from 2002 to 2017[9].

83 Based on literature records and data analysis, the last local malaria case in Handan  
84 was occurred before 2005. In the last decades, notified malaria infections have been  
85 entirely imported. There was no documented cases by autochthonous transmission, and  
86 it mainly related to the improvement of public health care and a strong sense of personal  
87 health. Although there is a partial distribution of the potential vector of this species, it  
88 is considered that the current risk of introduced malaria is very low[17]. In order to

89 improve knowledge about malaria-imported cases characteristics, the epidemiological  
90 and clinical characteristics of patients diagnosed with malaria in Handan were assessed.

91 In this study, an epidemiological investigation of every case of imported malaria in  
92 Handan was conducted. We have a systematic analysis of the key components of  
93 malaria surveillance, including trends in malaria prevalence, the origin of imported  
94 malaria, the Plasmodium species, and prevention effects of malaria.

## 95 **Methods**

### 96 **Study site**

97 Handan city is located in the southern end of Hebei Province and in the northern part  
98 of China, laying between latitudes 36°20` and 36°40`N, and longitude 114°03` and  
99 114°40`E. The total area is 12047 square kilometers, of which the mountainous area is  
100 4460 square kilometers, the plain area is 7587 square kilometers. It has a population of >  
101 9.5 million and includes 18 counties. Handan belongs to the southeast monsoon climate  
102 region, which is a continental monsoon climate transiting from the semi-humid zone of  
103 warm zone to the semi-arid zone. It has abundant sunshine, the same period of rain and  
104 heat, the same period of dry and cold, and the four seasons are alternating obviously.  
105 The main cash crops wheat, maize, cotton, millet, rice and soybean. This variety in  
106 climate, environment, and ecology makes the area favourable for mosquitoes.

### 107 **Study design**

108 The data were obtained from the national malaria surveillance system, including two  
109 systems: National notifiable infectious disease reporting information system and  
110 Malaria enhanced surveillance information system, and compilation of information on

111 the elimination of malaria, (i.e., epidemic situation reports, individual case information  
112 reports and assessment reports of malaria elimination).

### 113 **Fever patient blood smear microscopy**

114 Since 2010, microscopic examinations on “triple fever” patients (clinically diagnosed  
115 as having malaria, suspected malaria or unexplained fever) have been carried out each  
116 year. And blood tests have been conducted for malaria parasites.

### 117 **Mosquito collection and species identification**

118 Light-traps without bait and landing count method were used to capture mosquitoes.  
119 After being transferred to the laboratory, the mosquitoes were morphologically divided  
120 into *Anopheles*, *Culex*, *Aedes*, and other subfamilies or genera. The species of  
121 *Anopheles* were further classified by morphology[18].

### 122 **Data analysis**

123 All data analysis was conducted by the Statistical Package for Social Sciences software  
124 (version 22.0; SPSS Inc., IL, USA).

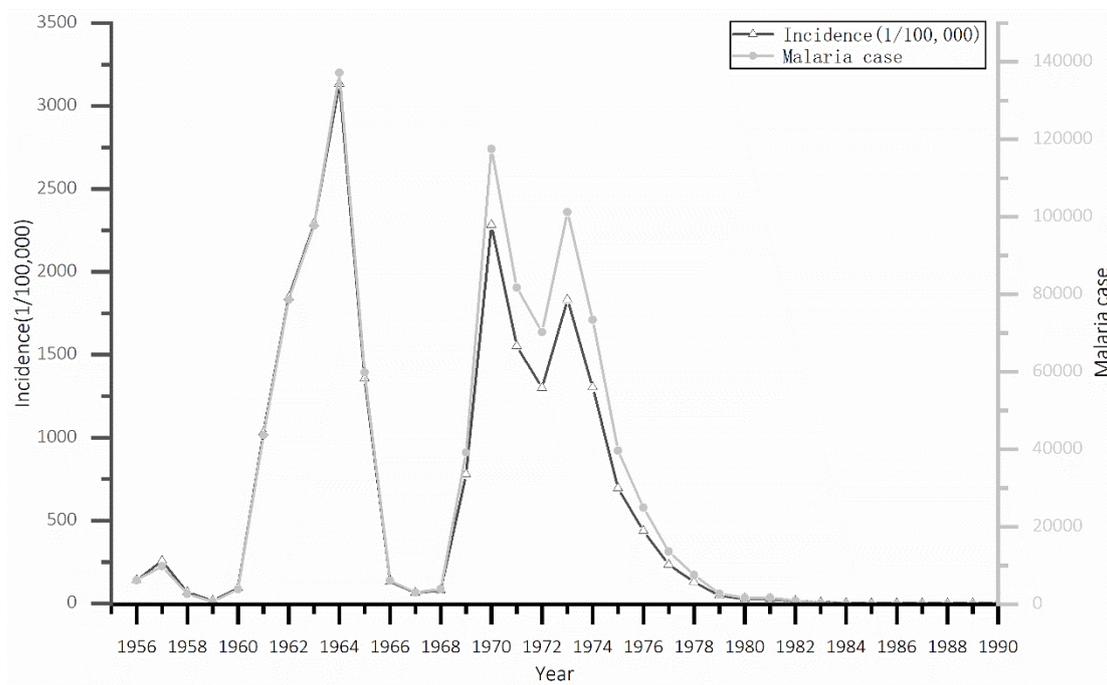
## 125 **Results**

### 126 **Descriptive analysis of the malaria cases**

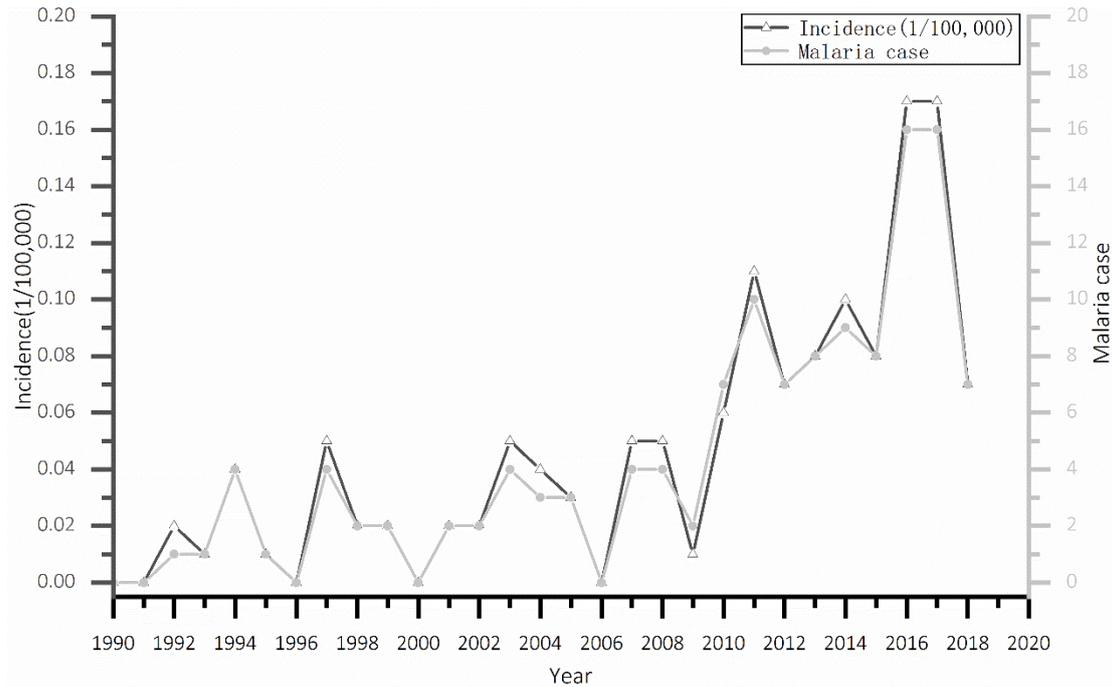
#### 127 *Occurrence of cases*

128 In the 1960s and 1970s, Handan city experienced widespread malaria outbreaks, which  
129 was in line with the provincial and national epidemic patterns. From 1956 to 2010, a  
130 total of 1029532 malaria cases were reported in Handan city, accounting for more than  
131 11% of the total malaria cases in Hebei province during the same period. The  
132 prevalence of malaria was mainly from the 1950s to the 1980s, and the average

133 incidence of malaria in each decade was 119.9/100 000, 1079.8/100 000, 980.5/100 000  
 134 and 7.7/100 000, respectively. During this period, there were three epidemic peaks in  
 135 Handan city, respectively in 1964, 1970 and 1973, and the reported incidence was as  
 136 high as 3135.5/100 000, 2281.9/100 000 and 1833.0/100 000, respectively. After 1973,  
 137 the annual incidence of malaria declined rapidly. By 1985, the annual reported  
 138 incidence of malaria in Handan city had dropped to less than 1/100 000 (Figure 1A).



139  
 140 Figure 1A Malaria incidence and cases reported in Handan, Hebei Province from 1956  
 141 to 1990.



142

143 Figure 1B Malaria incidence and cases reported in Handan, Hebei Province from 1991  
 144 to 2018.

145 During 1989-2010, 47 cases of malaria were reported in the early malaria elimination  
 146 phase. The highest incidence rate was 2010 (0.06/100 000), and no malaria cases were  
 147 reported in 1990, 1991, 1996, 2000 and 2006. In the eradication phase between 2011  
 148 and 2018, a total of 81 imported cases of malaria were reported (Figure 1B). After 2009,  
 149 there was an increase in fluctuation of malaria cases imported from other countries.

150 *Determinaton/Judgement of the final indigenous case*

151 All 81 malaria cases reported in Handan City from 2011 to 2018 had detailed  
 152 epidemiological records, and all of them had a detailed history of living in high malaria  
 153 areas abroad, which could rule out the possibility of local infection.

154 From 2005 to 2010, there were 17 cases of malaria in Handan city, 5 cases of  
 155 *plasmodium falciparum* malaria, 2 cases of *plasmodium vivax* malaria, 1 case of mixed  
 156 infection of *P. vivax* and *P. falciparum* malaria, and 9 cases of unclassified malaria.

157 Since our city was historically an endemic area of *P. vivax* and no *P. falciparum* malaria  
 158 vector existed, we determined that the *P. falciparum* cases were imported cases. A  
 159 retrospective investigation was conducted on the outward travel history of 2 cases of *P.*  
 160 *vivax* malaria and 9 cases of unclassified malaria. The survey confirmed they all had  
 161 experience of working in malaria-infected areas in south China or abroad. According  
 162 to the above investigation results, it can be concluded that the last indigenous case in  
 163 Handan city occurred before 2005.

164 **Plasmodium species composition**

165 From 1956 to 2018, four species of *plasmodium* (*P. vivax*, *P. falciparum*, *P. ovale* and  
 166 *P. malariae*) were identified in 1029613 malaria cases. Prior to 1988, all cases of  
 167 malaria were caused by *P. vivax* infection and included 1029485 cases. From 1989 to  
 168 2010, a total of 47 cases of malaria have been reported. And one *P. falciparum* case and  
 169 one unclassified *Plasmodium* case has been reported in 2007. From 2011 to 2018, 55  
 170 cases of *P. falciparum* accounted for 67.9% of the total malaria infections. In addition,  
 171 three cases of *P. ovale* infection and one case of *P. malariae* infection was identified  
 172 during this period. Furthermore, there were nine unclassified *plasmodium* infections  
 173 (Table 1).

174 Table 1 *Plasmodium* species in Handan city, 1956-2018

Year	<i>P. vivax</i>	<i>P. falciparum</i>	<i>P. ovale</i>	<i>P. malariae</i>	Mixed	Unclassified	Total
1956-1970	609778	0	0	0	0	0	609778

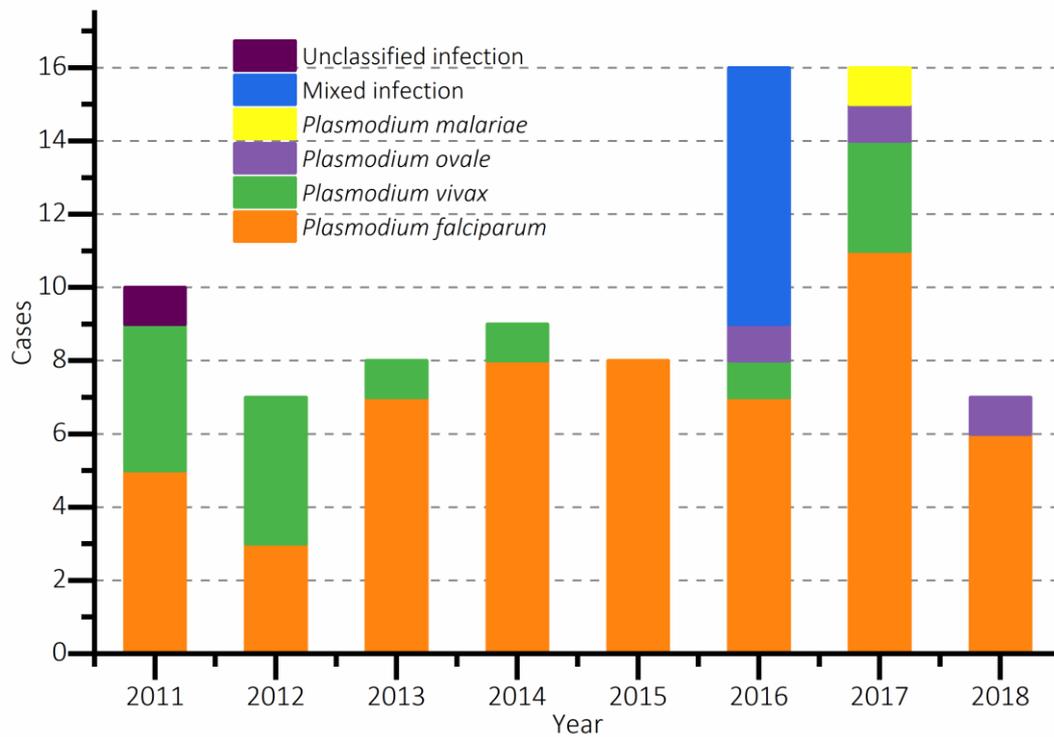
1971- 1988	419707	0	0	0	0	0	419707
1989- 2006	30	0	0	0	0	0	30
2007- 2018	17	61	3	1	7	9	98
Total	1029532	61	3	1	7	9	1029613

175

176 **Patterns of imported case in malaria elimination stage**

177 *General epidemiologic profile*

178 Among the 81 cases, there were 14 cases of *P. vivax*, 55 cases of *P. falciparum*, 3 cases  
 179 of *P. ovale*, 7 cases of *P. falciparum* and *P. ovale* mixed infection, 1 case of *P. malariae*,  
 180 and 1 case of unclassified during 2011-2018 (Figure 2). Of these, 37 cases were  
 181 reported locally and 44 were reported from other cities. The demographic features of  
 182 imported cases in 2011-2018 was shown in Table 2. All of the imported malaria cases  
 183 were male. The 21-50 age group had the most malaria cases, accounting for 91.4% of  
 184 the total 81 cases. The remaining age groups of 20 years or less and 51 years or more  
 185 included only a small number of cases, 1 and 6, respectively. The proportion of farmers,  
 186 oversea laborers and workers was the highest, accounting for 43.2% (35/81), 24.7%  
 187 (20/81) and 19.8% (16/81) of the total occupation distribution, respectively.



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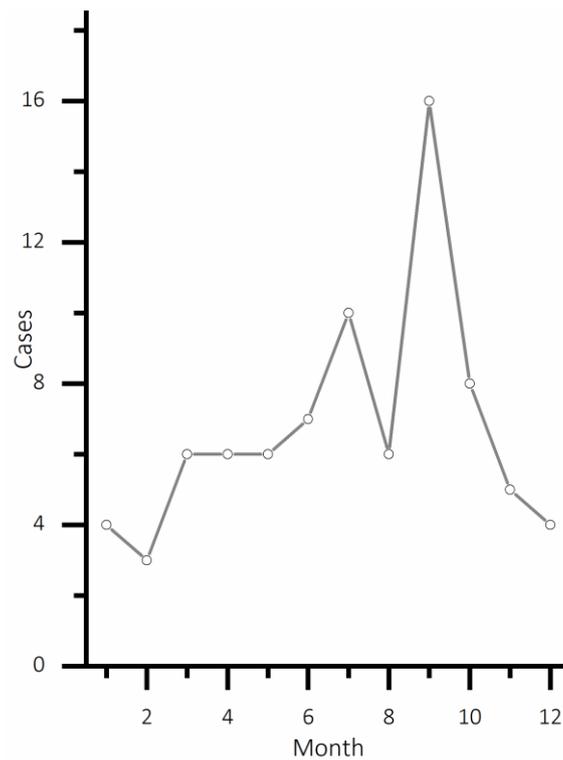
189 Figure 2 Species type distribution of imported malaria in Handan city from 2011 to  
190 2018.

191 Table 2 Demographic characteristic of malaria cases in Handan city between 2011 and  
192 2018.

Variables	2011	2012	2013	2014	2015	2016	2017	2018	Total
Male	10	7	8	9	8	16	16	7	81
≤20	0	0	1	0	0	0	0	0	1
21-50	10	7	7	9	7	15	14	5	74
≥51	0	0	0	0	1	1	2	2	6
Farmers	1	1	5	5	3	11	9	0	35
Oversea laborers	8	3	0	2	3	3	1	0	20
Workers	1	0	1	1	1	1	4	7	16

Houseworker	0	1	2	0	1	0	0	4
Businessmen	0	1	0	1	0	1	0	3
Others	0	1	0	0	0	0	2	3

193 \*Others include cadres, Individual worker, for example.



194

195 Figure 3 Monthly distribution of imported malaria in Handan city during the period of  
 196 2011-2018.

197 The onset time of imported malaria was not related to the season. Cases reported in  
 198 every month during 2011-2018. There were 10 cases in July and 16 cases in September,  
 199 and 3-8 cases in other months, which was consistent with the time of overseas return of  
 200 the cases (Figure 3). In addition, the 8-year cases analysis displayed that most of these  
 201 cases were recorded in the counties of Chengan, Linzhang, Weixian and the main city  
 202 zone of Handan, which reported 41, 8, 5 and 8 cases of imported malaria, respectively,  
 203 which accounted for 76.5% of the total number of cases. All the imported cases had

204 work experience abroad before their onset. Among them, 22 cases were from Nigeria  
205 and 20 cases from Congo, accounting for 51.8%. Angola, Pakistan and Myanmar  
206 followed with 5, 6 and 5 cases, respectively. The results of epidemiological  
207 investigation showed that all the cases were imported from abroad.

#### 208 *Case investigations*

209 All 37 cases were investigated by malaria control personnel of the disease control  
210 institutions in their jurisdiction, and the samples of cases were rechecked by county,  
211 city and provincial CDC. After a laboratory confirmed malaria case, the municipal  
212 CDC provides the patient with antimalarial drugs. The clinician is responsible for the  
213 treatment of the patient, and the malaria control personnel in the district are responsible  
214 for the follow-up of the treatment progress and results of the case. In view of the  
215 historical prevalence of *P. vivax* in our city, and the occasional capture of *Anopheles*  
216 *sinensis* (*An. sinensis*) in mosquito density monitoring in recent years, we determined  
217 the living places of these 9 *P. vivax* cases to be the epidemic sites with the possibility  
218 of transmission, and carried out key treatment according to the disposal requirements.  
219 *An. sinensis* and other malaria mosquitoes were not found by vector investigation, and  
220 no suspicious cases were found in active screening of fever cases. The standard disposal  
221 rate of the epidemic site was 100%, and no imported secondary cases of locally infected  
222 malaria were detected.

#### 223 *Fever patient blood tests*

224 According to province program requirements, the number of blood fever patients  
225 between 2011 and 2018 was higher than blood tests required. Except for 2011, the

226 completion rate of blood tests was more than 100%, and the proportion of blood tests  
 227 in the transmission season reached 50%. Since 2010, Handan has been actively  
 228 managing patients who are currently ill. 81 malaria cases were treated, including 37  
 229 locally reported imported cases, and all cases were in good condition after treatment  
 230 (Table 3).

231 Table 3 The number of blood tests and patient treated in Handan city, 2011-2018

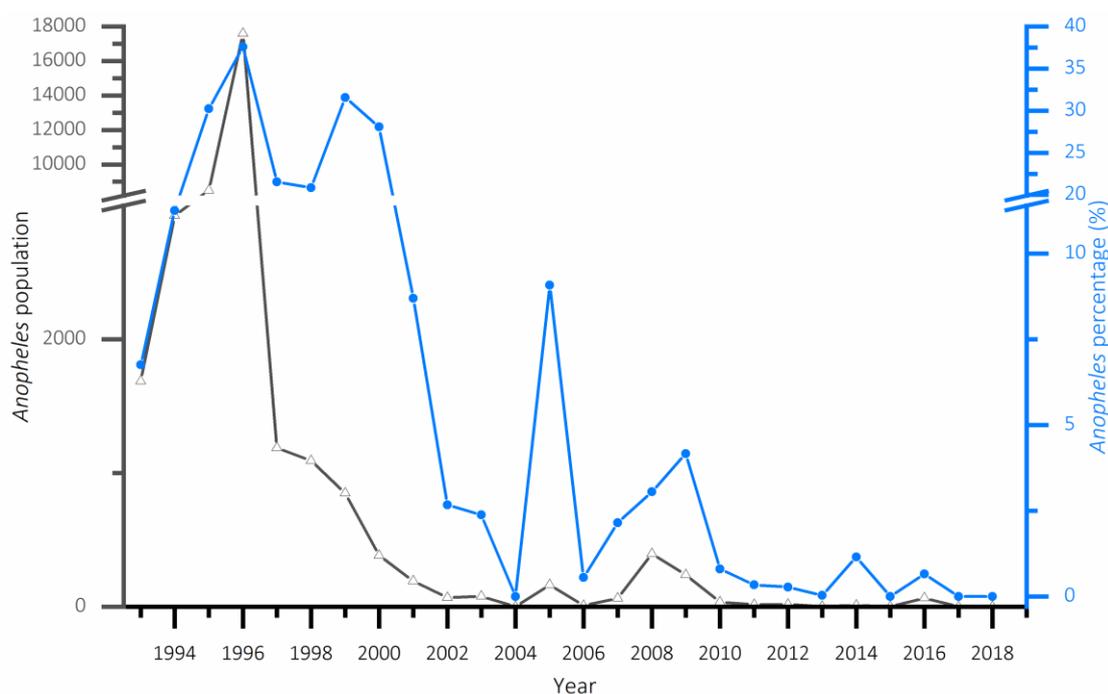
Year	Blood tests required	Completed blood tests	Complete percentage (%)	Percentage (%) in 5-10 months	Check consistency (%)	Case number
2011	16387	13391	81.7	61.7	100%	8
2012	4213	4689	111.3	79.1	100%	3
2013	4389	5302	120.8	83.3	100%	1
2014	4389	5378	122.5	82.4	100%	4
2015	4389	5172	117.84	81.4	100%	3
2016	950	1073	113.0	50.0	100%	7
2017	900	1046	116.2	53.4	100%	8
2018	900	1214	134.9	62.3	100%	3
Total	36517	37265				37

232

### 233 Vector investigations

234 During the malaria epidemic in the 20th century, all the malaria cases in Hebei province  
 235 were *p. vivax*, and *An. sinensis* was the only malaria vector. Traceable vector

236 monitoring data in Handan city began in the 1950s. There were 18 species of adult  
 237 mosquitoes from 3 genera and 18 species of larvae. Except *An. sinensis*, no other species  
 238 of malaria vector were found. The main breeding places of *An. sinensis* are concentrated  
 239 in rice fields and its irrigation systems. According to the number of *An. sinensis*  
 240 specimens and the date and place of collection, *An. sinensis* is a common mosquito  
 241 species in Handan City. Before the year of 1993, rice cultivation area in the Fu River  
 242 and Qing Zhang River basin was large. With the rapid social development, rice  
 243 cultivation has been greatly reduced since 2003. Now, there are almost no paddy fields,  
 244 but mainly wheat and corn.



245  
 246 Figure 4 *Anopheles* number and *Anopheles* percentage accounting for the captured  
 247 mosquitoes in Handan, Hebei Province in the 1993-2018 period.

248 Since 1993, mosquito vector monitoring has been carried out continuously in the  
 249 main urban area of Handan, the annual mosquito density fluctuates greatly, but the  
 250 overall trend is decreasing, and it is related to the annual precipitation (Figure 4). In

251 1996, during the flood disaster in Handan City, the highest number of *An. sinensis*  
252 mosquitoes were captured, with a density of 251.3 mosquitoes per night lamp,  
253 accounting for 37.6% of the captured mosquitoes. After that, both the density and  
254 proportion of *Anopheles* mosquitoes showed a decreasing trend. According to the  
255 monitoring results from 2003 to 2015, the composition ratio and capture number of *An.*  
256 *sinensis* have decreased significantly since 2010. The density of mosquitoes, the density  
257 of *Anopheles* and the proportion of *Anopheles* increased slightly during the floods in  
258 Handan City in the summer of 2016. Subsequently, *An. sinensis* was not caught in 2017  
259 and 2018.

## 260 **Discussion**

261 Handan used to be an area of high prevalence of *P. vivax*, with *An. sinensis* as the single  
262 vector. The rivers in Handan are Ming River in the north, Fuyang River in the middle  
263 and Zhang River in the south. At present, Fuyang River has water all the year round,  
264 and Ming River and Zhang River are in a dry period. However, tributaries with reeds,  
265 irrigation ditches, ponds and drains around villages are the best breeding grounds for  
266 *An. sinensis*. And people who live nearby are more likely to get bitten by mosquitoes  
267 during peak biting times, which can lead to malaria. In Handan City, corn and wheat  
268 are the main crops. In the 1970s, Fuyang River basin began to introduce rice planting  
269 and formed a scale of water field; with the reduction of surface water resources and  
270 ecological environment control, water field has been basically disappeared by the end  
271 of the 1990s. This is also a good fit with the malaria epidemic trend in our city.

272 During the epidemic stage (1956-1985), the incidence of malaria in Handan was

273 obviously seasonal, with high incidence from May to September. With the increase of  
274 national efforts to prevent and control infectious diseases and the improvement of the  
275 environment, the incidence of malaria dropped to sporadic levels in the late 1980s. The  
276 incidence was non-seasonal, and cases were reported even in winter and spring when  
277 mosquitoes were not active. From 1989 to 2004, a total of 27 malaria cases were  
278 reported. Due to the lack of relevant epidemiological data, it is impossible to verify  
279 whether the malaria cases reported during this period were locally infected.

280 A total of 20 malaria cases were reported in 2005-2010. According to the case  
281 information, there was a clear history of living in areas with high malaria in foreign  
282 countries and they were imported cases. From 2011 to 2018, 81 cases were reported,  
283 all of which had detailed epidemiological investigation information and were imported  
284 from abroad. The number of imported malaria cases increased during this period, which  
285 was consistent with the increase of export channels and personnel of labor services  
286 abroad. In this period, malaria elimination efforts will focus on the management of  
287 malaria patients, the maintenance of blood testing capacity for malaria parasites in  
288 patients with fever, and the screening and investigation of people traveling to and from  
289 areas with high malaria levels.

290 Since the implementation of the malaria elimination work in our city, the malaria  
291 prevention and control work has achieved remarkable results, which has improved the  
292 people's knowledge of malaria and self-prevention ability, and greatly enhanced the  
293 medical institutions' ability to treat malaria cases. The indicators reached the standard  
294 of eliminating malaria. To maintain this goal, the following points need to be noted.

295 With socio-economic development, urban expansion has accelerated and regional  
296 ecological changes have resulted in a decrease in malaria cases and the elimination of  
297 indigenous cases, this point was confirmed in the study of Wang *et al.* Wang reported  
298 that malaria prevention and control measures and local fiscal revenue increases were  
299 related to the decrease of malaria incidence in Hainan [19].

300 In 2017, China reported zero indigenous malaria case for the first time. In addition,  
301 zero indigenous malaria case was reported in the Chinese mainland for three  
302 consecutive years from 2017 to 2019 [9]. However, malaria cases imported from Africa  
303 and Southeast Asia are still occurring in China because of overseas labor [20, 21].  
304 Therefore, country-led efforts are regional and intersectoral cooperation and ongoing  
305 monitoring and evaluation. Meanwhile, some works must be done consistently, such as  
306 the maintenance of non-transmission status, the diagnosis, treatment and management  
307 of imported malaria cases, the implementation of business training, technical guidance,  
308 quality control and supervision and inspection, through multi-sectoral collaboration [22,  
309 23].

310 Maintaining the microscopic capability of primary health inspectors is also a  
311 challenge in achieving and sustaining malaria eradication [24]. In 2011, the completion  
312 rate of blood tests was 81.7% (13391/16387), and there were nine unclassified  
313 *plasmodium* infections during 2007-2018. Hence, the skills of microscopists for the  
314 preparation and interpretation of blood smears should be strengthened. In order to keep  
315 the eradication of malaria sustainable, we will take precise measures at different levels  
316 and areas. The Internet and other technological means should be used to enhance the

317 level of information technology and improve the effectiveness of the prevention[25].  
318 The prevention and control of malaria should be scientifically divided and precisely  
319 controlled.

### 320 **Conclusions**

321 Our study found that the source of malaria case detection has changed greatly from the  
322 control to elimination stage, and the individual case-based malaria surveillance system  
323 generally worked well in the malaria elimination stage in Handan, China. However,  
324 Handan still faces many challenges, including epidemiological changes in malaria cases  
325 among the international migrant workers and hard-to-reach populations.

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### 330 **Authors' contributions**

331 RG, ZJ conducted the study design and study implementation. RG, SL, ZJ performed  
332 the data analyses and draft the manuscript. RG, JZ, YL, JD, XW, JL, SL, ZJ provided  
333 public health insight for analyzing the results. All authors read, edited and approved the  
334 final manuscript.

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### 338 **Data availability**

339 Not applicable.

340 **Ethical approval**

341 Not required.

342 **Consent for publication**

343 Not applicable.

344 **Competing interests**

345 The authors declare that they have no competing interests.

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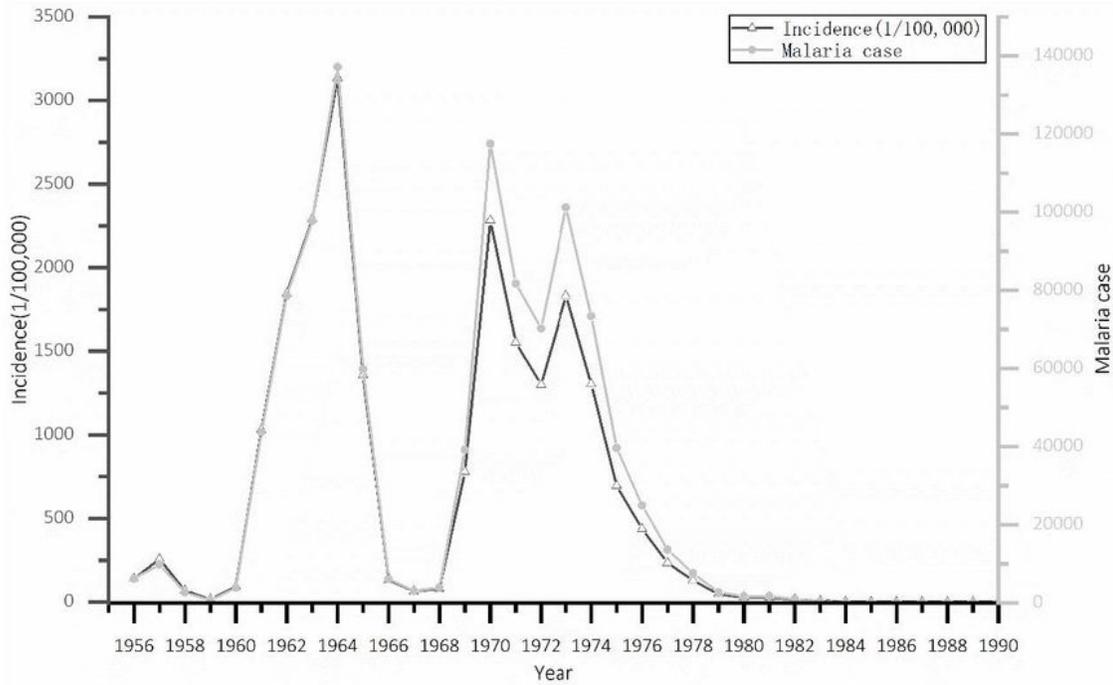
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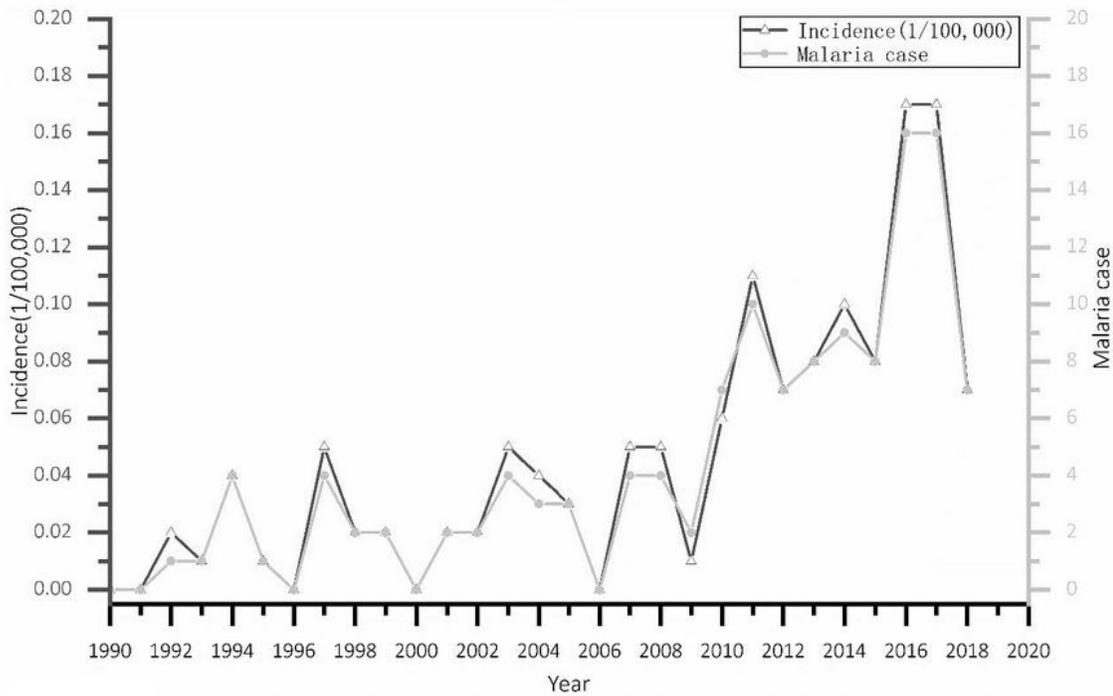
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# Figures



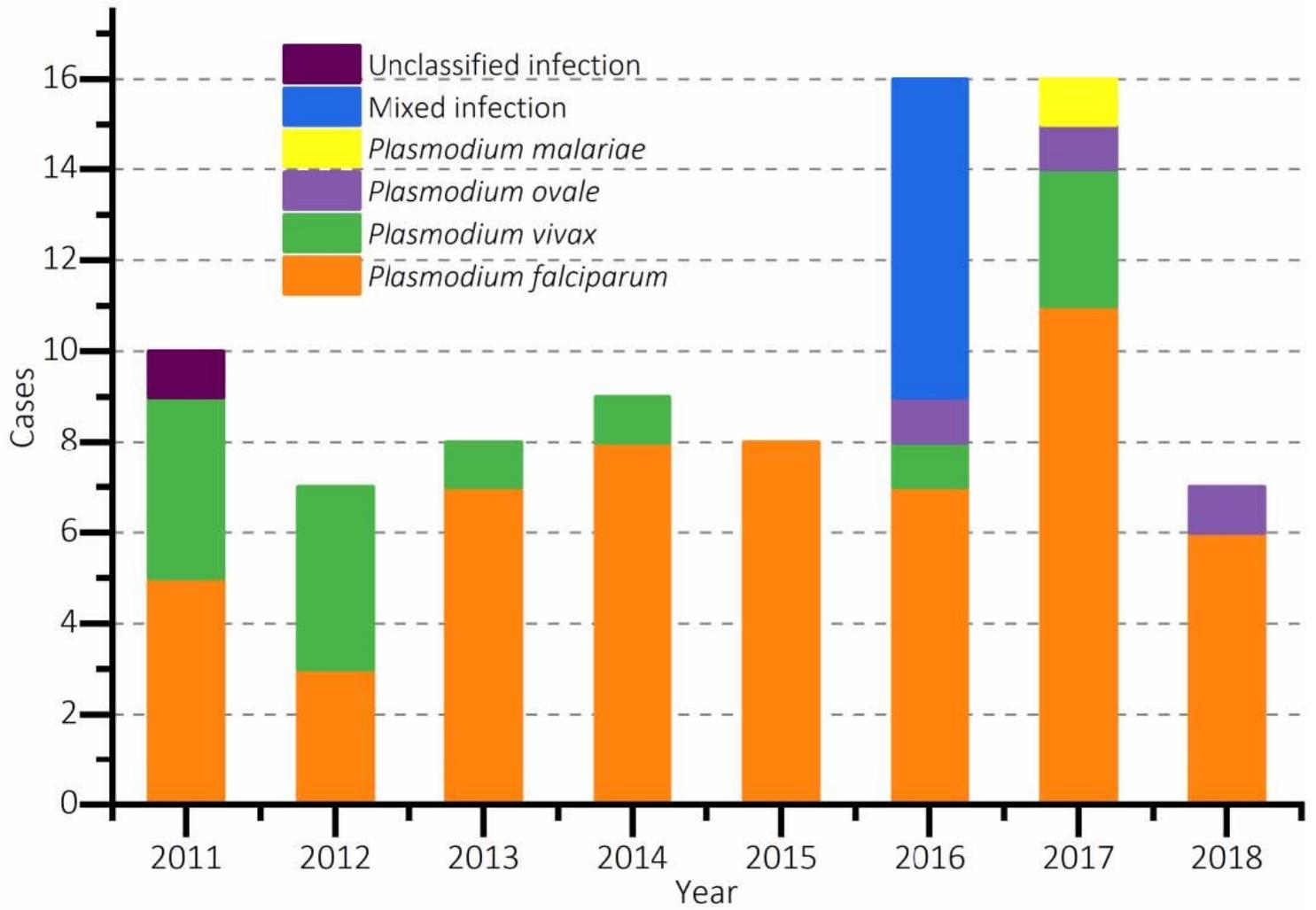
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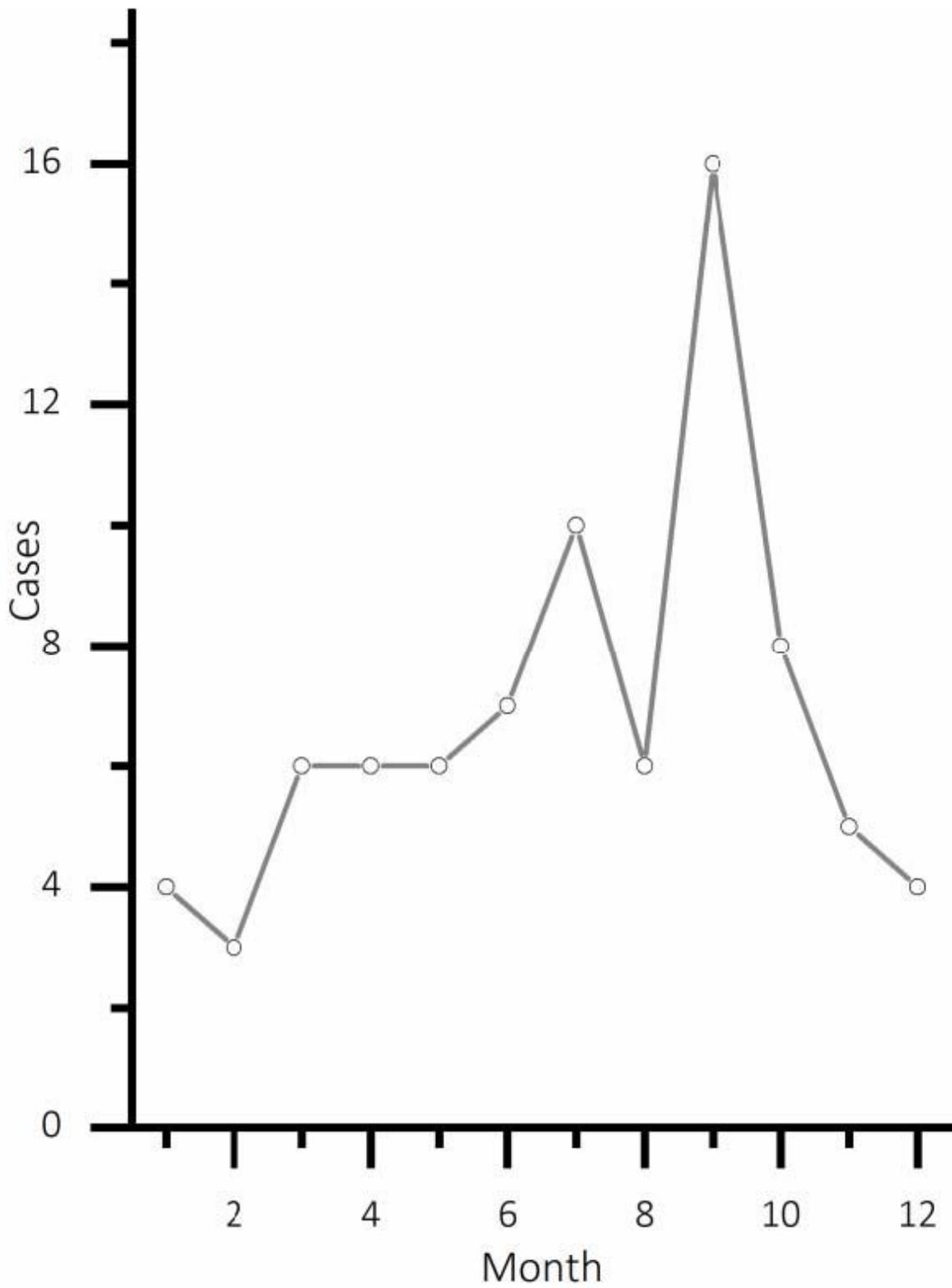
Figure 1

1A Malaria incidence and cases reported in Handan, Hebei Province from 1956 to 1990. 1B Malaria incidence and cases reported in Handan, Hebei Province from 1991 to 2018.



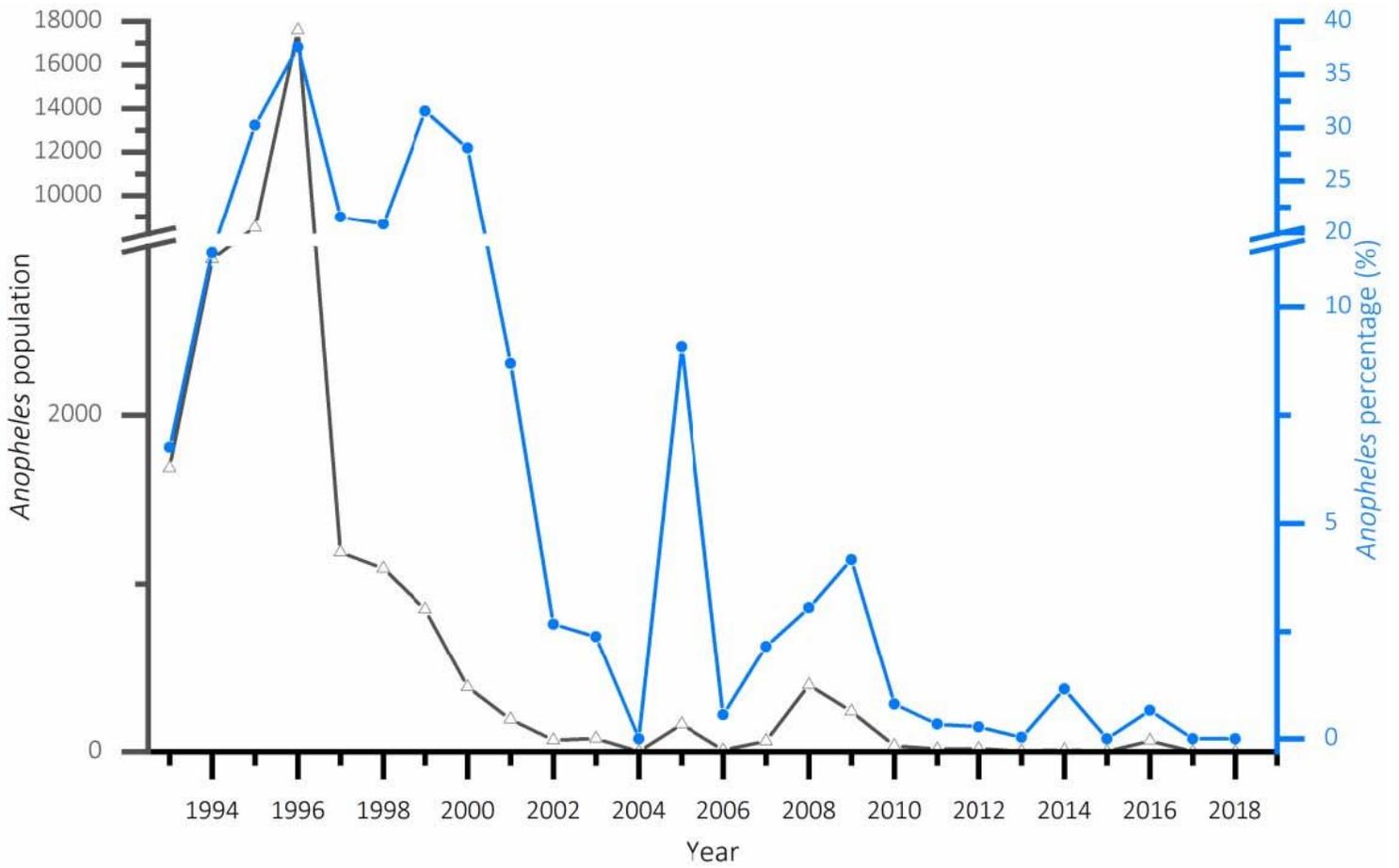
**Figure 2**

Species type distribution of imported malaria in Handan city from 2011 to 2018.



**Figure 3**

Monthly distribution of imported malaria in Handan city during the period of 2011-2018.



**Figure 4**

Anopheles number and Anopheles percentage accounting for the captured mosquitoes in Handan, Hebei Province in the 1993-2018 period.