

Analysis of Epidemiological Changes and Elimination Effects for Malaria in North China

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**Analysis of epidemiological changes and elimination effects for malaria in North
China**

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23 **Abstract**

24 **Background:** The elimination of malaria requires high-quality surveillance data in
25 order to detect and respond quickly to individual cases. In the 1960s and 1970s,
26 Handan city in North China experienced widespread malaria outbreaks, which was in
27 line with the provincial and 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
33 city, China. From 2011 to 2018, 81 malaria cases were reported in Handan city, all of
34 which were imported from abroad. The annual average incidence decreased to
35 0.11/100 000 in the elimination stage, while all malaria cases were male. Since the
36 initiation of the National Malaria Elimination Programme in 2010, malaria cases were
37 consistent with the increase in overseas export channels and personnel of labor
38 services.

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

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

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44

45 **Backgroud**

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

61 In the past, especially in the last 30-40 years after the founding of the People's
62 Republic of China, China has suffered from severe malaria epidemics[7]. From 1949
63 to 2020, the transmission of the malaria can be primarily divided into four phases:
64 transmission; outbreak and pandemic transmission; decline with sporadic distribution;
65 and the elimination phase[8]. A national malaria elimination programme (NMEP) was
66 launched in China in 2010, which surports to achieve zero indigenous case of malaria

67 within the 2020 timeline[9]. The elimination phase is different from the control phase,
68 and needs to monitor and respond to each malaria infection, and to eventually stop
69 local malaria transmission. China has developed a case-based malaria surveillance
70 system to gather information needed for diagnosis and investigation, and to promote a
71 rapid response to individual cases[10, 11]. In order to eliminate malaria, the strengths
72 and limitations of the program must be understood by quantitatively evaluating the
73 performance and efficiency of NMEP[12, 13].

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

85 Given an example, Handan city (2018 population 9.52 million), a typical northern
86 city with a long history in North China. Based on literature records and data analysis,
87 the last local malaria case in Handan was occurred before 2005. In the last decades,
88 notified malaria infections have been entirely imported. There was no documented

89 cases by autochthonous transmission, and it mainly related to the improvement of
90 public health care and a strong sense of personal health. Although there is a partial
91 distribution of the potential vector of this species, it is considered that the current risk
92 of introduced malaria is very low[17]. In order to improve knowledge about
93 malaria-imported cases characteristics, the epidemiological and clinical characteristics
94 of patients diagnosed with malaria in North China were assessed.

95 In this study, an epidemiological investigation of every case of imported malaria in
96 North China was conducted. We have a systematic analysis of the key components of
97 malaria surveillance, including trends in malaria prevalence, the origin of imported
98 malaria, the Plasmodium species, and prevention effects of malaria.

99 **Methods**

100 **Study site**

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

111 for mosquitoes.

112 **Study design**

113 The data were obtained from the national malaria surveillance system, including two
114 systems: National notifiable infectious disease reporting information system and
115 Malaria enhanced surveillance information system, and compilation of information on
116 the elimination of malaria, (i.e., epidemic situation reports, individual case
117 information reports and assessment reports of malaria elimination).

118 **Fever patient blood smear microscopy**

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

122 **Mosquito collection and species identification**

123 The lamp trap method was used. Methods According to the characteristics of
124 mosquito breeding and distribution, four representative areas with different habitats
125 were selected in residential areas, parks, hospitals, rural houses and cattle sheds in
126 three urban districts and rural suburbs of Handan. The survey will be conducted twice
127 a month from May to October every year. In the above time, one mosquito lamp was
128 used in each place. The monitoring began 30 minutes after sunset, and the captured
129 adult mosquitoes were collected continuously for 12 hours. The captured adult
130 mosquitoes were brought back to the laboratory and smoked with ether for
131 classification and identification.

132 Light-traps without bait and landing count method were used to capture mosquitoes.

133 After being transferred to the laboratory, the mosquitoes were morphologically
134 divided into *Anopheles*, *Culex*, *Aedes*, and other subfamilies or genera. The species of

135 *Anopheles* were further classified by morphology[18].

136 **Data analysis**

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

139 **Ethics approval and consent to participate**

140 The experimental research reported in the current study was performed with the
141 approval of the Ethics Committee of the Handan Municipal Centre for Disease
142 Control and Prevention and the Ethics Committee of Hebei University of Engineering.
143 Human research was performed in compliance with the Declaration of Helsinki and
144 its later amendments. All participants provided their written informed consent to
145 participate in this research.

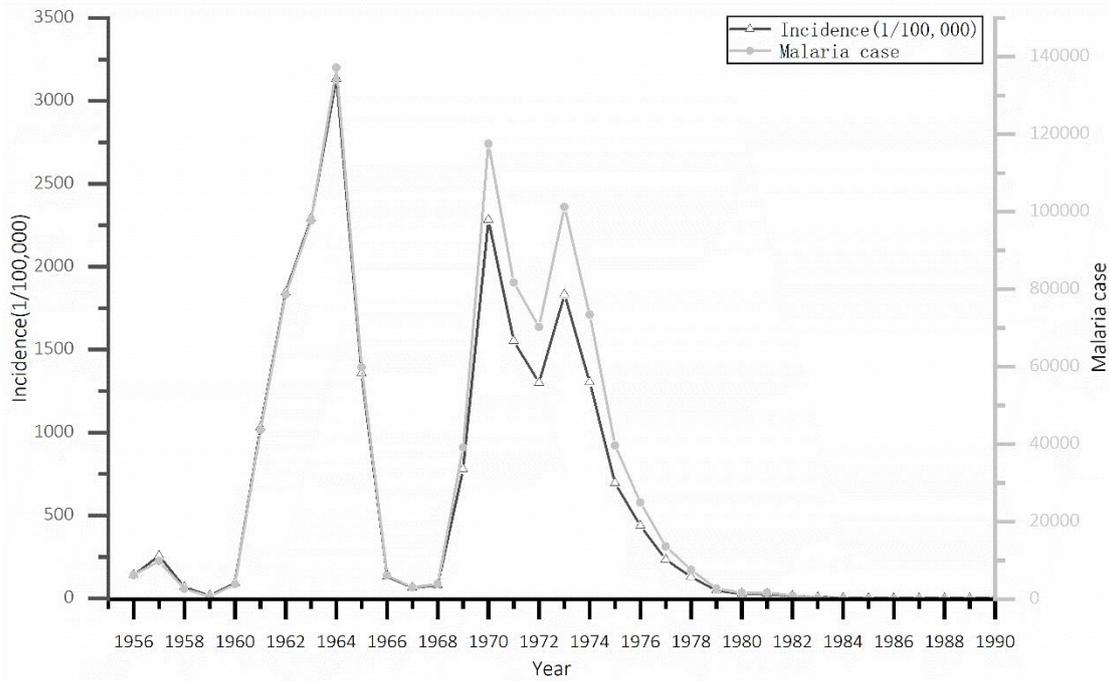
146 **Results**

147 **Descriptive analysis of the malaria cases**

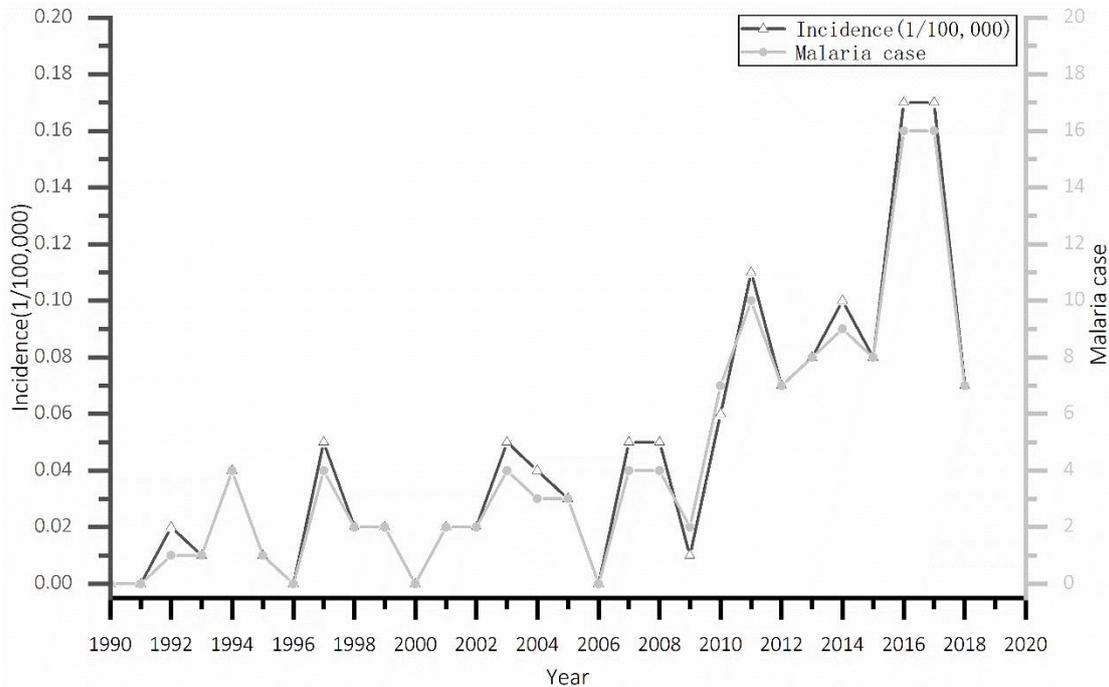
148 *Occurrence of cases*

149 In the 1960s and 1970s, Handan city experienced widespread malaria outbreaks,
150 which was in line with the provincial and national epidemic patterns. From 1956 to
151 2010, a total of 1029532 malaria cases were reported in Handan city, accounting for
152 more than 11% of the total malaria cases in North China during the same period. The
153 prevalence of malaria was mainly from the 1950s to the 1980s, and the average
154 incidence of malaria in each decade was 119.9/100 000, 1079.8/100 000, 980.5/100
155 000 and 7.7/100 000, respectively. During this period, there were three epidemic
156 peaks in Handan city, respectively in 1964, 1970 and 1973, and the reported incidence
157 was as high as 3135.5/100 000, 2281.9/100 000 and 1833.0/100 000, respectively.
158 After 1973, the annual incidence of malaria declined rapidly. By 1985, the annual

159 reported incidence of malaria in Handan city had dropped to less than 1/100 000
 160 (Figure 1A).



161
 162 Figure 1A Malaria incidence and cases reported in Handan, Hebei Province from
 163 1956 to 1990.



164
 165 Figure 1B Malaria incidence and cases reported in Handan, Hebei Province from

166 1991 to 2018.

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

173 *Determinaton/Judgement of the final indigenous case*

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

177 From 2005 to 2010, there were 17 cases of malaria in Handan city, 5 cases of
178 *plasmodium falciparum* malaria, 2 cases of *plasmodium vivax* malaria, 1 case of
179 mixed infection of *P. vivax* and *P. falciparum* malaria, and 9 cases of unclassified
180 malaria. Since our city was historically an endemic area of *P. vivax* and no *P.*
181 *falciparum* malaria vector existed, we determined that the *P. falciparum* cases were
182 imported cases. A retrospective investigation was conducted on the outward travel
183 history of 2 cases of *P. vivax* malaria and 9 cases of unclassified malaria. The survey
184 confirmed they all had experience of working in malaria-infected areas in south China
185 or abroad. According to the above investigation results, it can be concluded that the
186 last indigenous case in Handan city occurred before 2005.

187 **Plasmodium species composition**

188 From 1956 to 2018, four species of *plasmodium* (*P. vivax*, *P. falciparum*, *P. ovale* and
 189 *P. malariae*) were identified in 1029613 malaria cases. Prior to 1988, all cases of
 190 malaria were caused by *P. vivax* infection and included 1029485 cases. From 1989 to
 191 2010, a total of 47 cases of malaria have been reported. And one *P. falciparum* case
 192 and one unclassified *Plasmodium* case has been reported in 2007. From 2011 to 2018,
 193 55 cases of *P. falciparum* accounted for 67.9% of the total malaria infections. In
 194 addition, three cases of *P. ovale* infection and one case of *P. malariae* infection was
 195 identified during this period. Furthermore, there were nine unclassified *plasmodium*
 196 infections (Table 1).

197 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

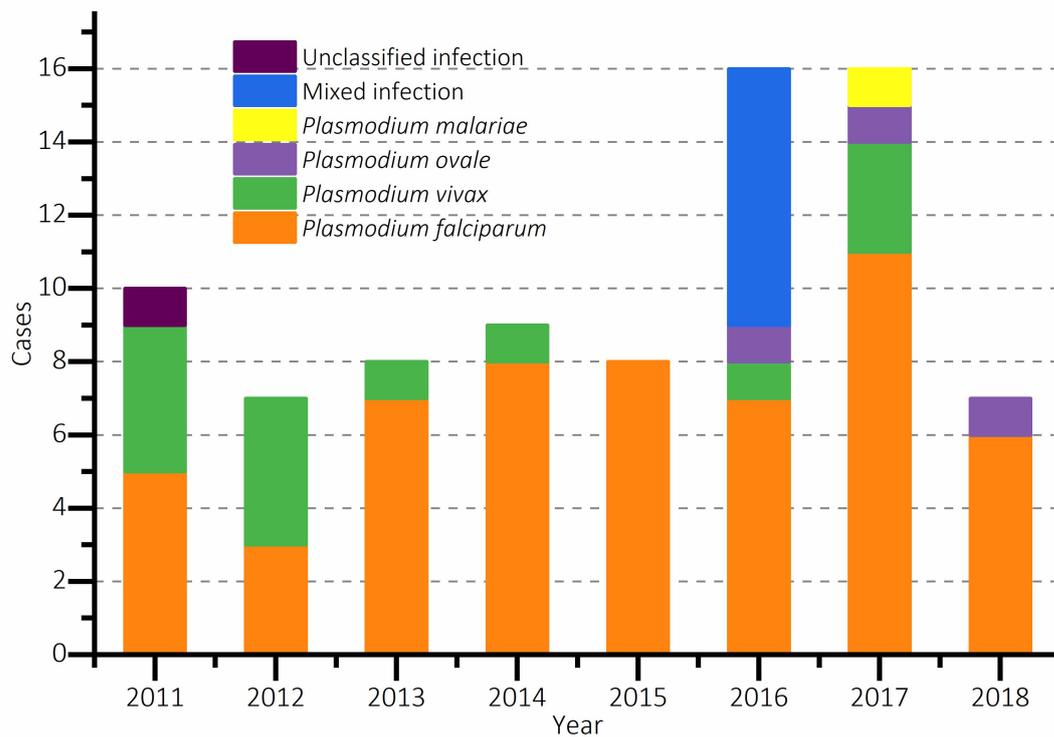
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199 **Patterns of imported case in malaria elimination stage**

200 *General epidemiologic profile*

201 Among the 81 cases, there were 14 cases of *P. vivax*, 55 cases of *P. falciparum*, 3
 202 cases of *P. ovale*, 7 cases of *P. falciparum* and *P. ovale* mixed infection, 1 case of *P.*

203 *malariae*, and 1 case of unclassified during 2011-2018 (Figure 2). Of these, 37 cases
 204 were reported locally and 44 were reported from other cities. The demographic
 205 features of imported cases in 2011-2018 was shown in Table 2. All of the imported
 206 malaria cases were male. The 21-50 age group had the most malaria cases, accounting
 207 for 91.4% of the total 81 cases. The remaining age groups of 20 years or less and 51
 208 years or more included only a small number of cases, 1 and 6, respectively. The
 209 proportion of farmers, oversea laborers and workers was the highest, accounting for
 210 43.2% (35/81), 24.7% (20/81) and 19.8% (16/81) of the total occupation distribution,
 211 respectively.

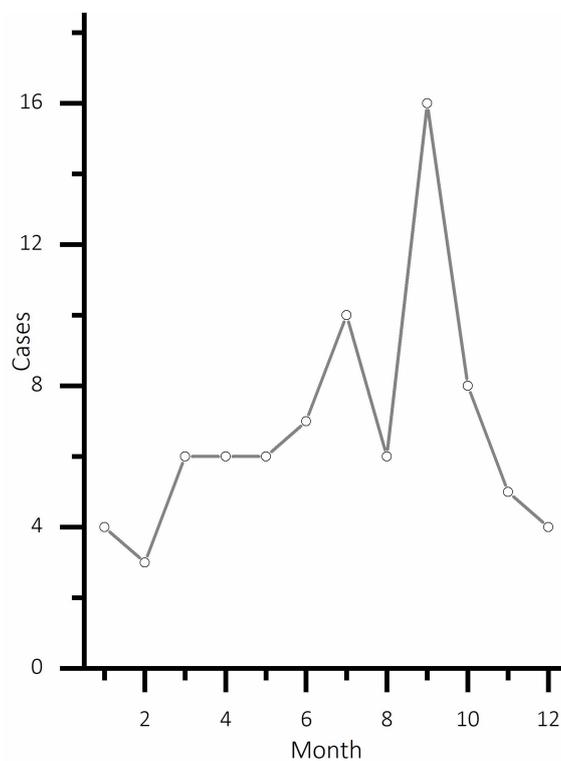


212
 213 Figure 2 Species type distribution of imported malaria in Handan city from 2011 to
 214 2018.

215 Table 2 Demographic characteristic of malaria cases in Handan city between 2011 and
 216 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	0	3

217 *Others include cadres, Individual worker, for example.



218

219 Figure 3 Monthly distribution of imported malaria in Handan city during the period of

220 2011-2018.

221 The onset time of imported malaria was not related to the season. Cases reported in
222 every month during 2011-2018. There were 10 cases in July and 16 cases in
223 September, and 3-8 cases in other months, which was consistent with the time of
224 overseas return of the cases (Figure 3). In addition, the 8-year cases analysis displayed
225 that most of these cases were recorded in the counties of Chengan, Linzhang, Weixian
226 and the main city zone of Handan, which reported 41, 8, 5 and 8 cases of imported
227 malaria, respectively, which accounted for 76.5% of the total number of cases. All the
228 imported cases had work experience abroad before their onset. Among them, 22 cases
229 were from Nigeria and 20 cases from Congo, accounting for 51.8%. Angola, Pakistan
230 and Myanmar followed with 5, 6 and 5 cases, respectively. The results of
231 epidemiological investigation showed that all the cases were imported from abroad.

232 *Case investigations*

233 All 37 cases were investigated by malaria control personnel of the disease control
234 institutions in their jurisdiction, and the samples of cases were rechecked by county,
235 city and provincial CDC. After a laboratory confirmed malaria case, the municipal
236 CDC provides the patient with antimalarial drugs. The clinician is responsible for the
237 treatment of the patient, and the malaria control personnel in the district are
238 responsible for the follow-up of the treatment progress and results of the case. In view
239 of the historical prevalence of *P. vivax* in our city, and the occasional capture of
240 *Anopheles sinensis* (*An. sinensis*) in mosquito density monitoring in recent years, we
241 determined the living places of these 9 *P. vivax* cases to be the epidemic sites with the

242 possibility of transmission, and carried out key treatment according to the disposal
 243 requirements. *An. sinensis* and other malaria mosquitoes were not found by vector
 244 investigation, and no suspicious cases were found in active screening of fever cases.
 245 The standard disposal rate of the epidemic site was 100%, and no imported secondary
 246 cases of locally infected malaria were detected.

247 *Fever patient blood tests*

248 According to province program requirements, the number of blood fever patients
 249 between 2011 and 2018 was higher than blood tests required. Except for 2011, the
 250 completion rate of blood tests was more than 100%, and the proportion of blood tests
 251 in the transmission season reached 50%. Since 2010, Handan has been actively
 252 managing patients who are currently ill. 81 malaria cases were treated, including 37
 253 locally reported imported cases, and all cases were in good condition after treatment
 254 (Table 3).

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

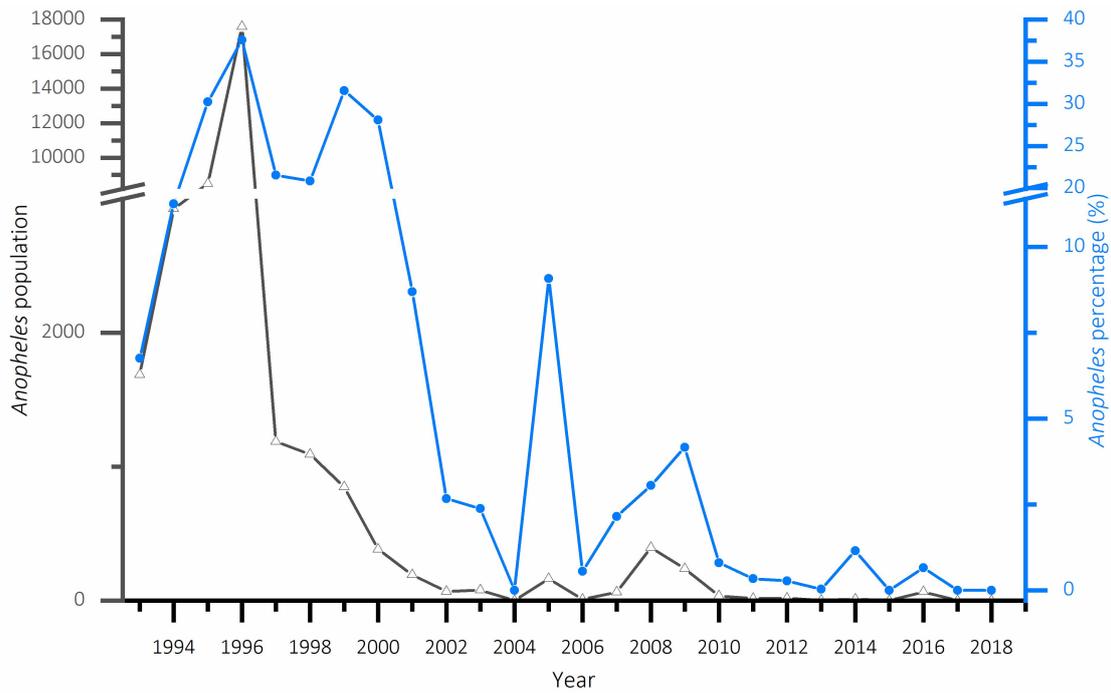
Year	Blood tests required	Completed blood tests	Complete percentage (%)	Percentage (%) in 5-10 months	Check consistency (%)	Case number
2011	16387	13391	81.7	61.7	100%	8
2012	4213	4689	111.3	79.1	100%	3
2013	4389	5302	120.8	83.3	100%	1
2014	4389	5378	122.5	82.4	100%	4
2015	4389	5172	117.84	81.4	100%	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

256

257 **Vector investigations**

258 During the malaria epidemic in the 20th century, all the malaria cases in Hebei
 259 province were *p. vivax*, and *An. sinensis* was the only malaria vector. Traceable vector
 260 monitoring data in Handan city began in the 1950s. There were 18 species of adult
 261 mosquitoes from 3 genera and 18 species of larvae. Except *An. sinensis*, no other
 262 species of malaria vector were found. The main breeding places of *An. sinensis* are
 263 concentrated in rice fields and its irrigation systems. According to the number of *An.*
 264 *sinensis* specimens and the date and place of collection, *An. sinensis* is a common
 265 mosquito species in Handan City. Before the year of 1993, rice cultivation area in the
 266 Fu River and Qing Zhang River basin was large. With the rapid social development,
 267 rice cultivation has been greatly reduced since 2003. Now, there are almost no paddy
 268 fields, but mainly wheat and corn.



269

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

272 Since 1993, mosquito vector monitoring has been carried out continuously in the
 273 main urban area of Handan, the annual mosquito density fluctuates greatly, but the
 274 overall trend is decreasing, and it is related to the annual precipitation (Figure 4). In
 275 1996, during the flood disaster in Handan City, the highest number of *An. sinensis*
 276 mosquitoes were captured, with a density of 251.3 mosquitoes per night lamp,
 277 accounting for 37.6% of the captured mosquitoes. After that, both the density and
 278 proportion of *Anopheles* mosquitoes showed a decreasing trend. According to the
 279 monitoring results from 2003 to 2015, the composition ratio and capture number of
 280 *An. sinensis* have decreased significantly since 2010. The density of mosquitoes, the
 281 density of *Anopheles* and the proportion of *Anopheles* increased slightly during the
 282 floods in Handan City in the summer of 2016. Subsequently, *An. sinensis* was not
 283 caught in 2017 and 2018.

284 **Discussion**

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

297 During the epidemic stage (1956-1985), the incidence of malaria in Handan was
298 obviously seasonal, with high incidence from May to September. With the increase of
299 national efforts to prevent and control infectious diseases and the improvement of the
300 environment, the incidence of malaria dropped to sporadic levels in the late 1980s.
301 The incidence was non-seasonal, and cases were reported even in winter and spring
302 when mosquitoes were not active. From 1989 to 2004, a total of 27 malaria cases
303 were reported. Due to the lack of relevant epidemiological data, it is impossible to
304 verify whether the malaria cases reported during this period were locally infected.

305 A total of 20 malaria cases were reported in 2005-2010. According to the case

306 information, there was a clear history of living in areas with high malaria in foreign
307 countries and they were imported cases. From 2011 to 2018, 81 cases were reported,
308 all of which had detailed epidemiological investigation information and were
309 imported from abroad. The number of imported malaria cases increased during this
310 period, which was consistent with the increase of export channels and personnel of
311 labor services abroad. In this period, malaria elimination efforts will focus on the
312 management of malaria patients, the maintenance of blood testing capacity for malaria
313 parasites in patients with fever, and the screening and investigation of people
314 traveling to and from areas with high malaria levels.

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

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

325 In 2017, China reported zero indigenous malaria case for the first time. In addition,
326 zero indigenous malaria case was reported in the Chinese mainland for three
327 consecutive years from 2017 to 2019 [9]. However, malaria cases imported from

328 Africa and Southeast Asia are still occurring in China because of overseas labor [20,
329 21]. Therefore, country-led efforts are regional and intersectoral cooperation and
330 ongoing monitoring and evaluation. Meanwhile, some works must be done
331 consistently, such as the maintenance of non-transmission status, the diagnosis,
332 treatment and management of imported malaria cases, the implementation of business
333 training, technical guidance, quality control and supervision and inspection, through
334 multi-sectoral collaboration [22, 23].

335 Maintaining the microscopic capability of primary health inspectors is also a
336 challenge in achieving and sustaining malaria eradication [24]. In 2011, the
337 completion rate of blood tests was 81.7% (13391/16387), and there were nine
338 unclassified *plasmodium* infections during 2007-2018. Hence, the skills of
339 microscopists for the preparation and interpretation of blood smears should be
340 strengthened. In order to keep the eradication of malaria sustainable, we will take
341 precise measures at different levels and areas. The Internet and other technological
342 means should be used to enhance the level of information technology and improve the
343 effectiveness of the prevention[25].

344 **Conclusions**

345 Our study found that the source of malaria case detection has changed greatly from
346 the control to elimination stage, and the individual case-based malaria surveillance
347 system generally worked well in the malaria elimination stage in North China. In the
348 long term, systematic vector surveillance to control adult mosquito density to less
349 harmful levels is also an important part of the post-elimination phase of malaria.
350 However, The North China still faces many challenges, including epidemiological
351 changes in malaria cases among the international migrant workers and hard-to-reach

352 populations.

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357 **Authors' contributions**

358 RG, ZJ conducted the study design and study implementation. RG, SL, ZJ performed
359 the data analyses and draft the manuscript. RG, JZ, XW, JL, WZ, SL, ZJ provided
360 public health insight for analyzing the results. All authors read, edited and approved
361 the final manuscript.

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366 **Data availability**

367 Not applicable.

368 **Ethical approval**

369 Not required.

370 **Consent for publication**

371 Not applicable.

372 **Competing interests**

373 The authors declare that they have no competing interests.

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375

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