

Imported malaria and high risk groups: observational study using UK surveillance data 1987-2006

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ABSTRACT

Objective To examine temporal, geographic, and sociodemographic trends in case reporting and case fatality of malaria in the United Kingdom.

Setting National malaria reference laboratory surveillance data in the UK.

Design Observational study using prospectively gathered surveillance data and data on destinations from the international passenger survey.

Participants 39 300 cases of proved malaria in the UK between 1987 and 2006.

Main outcome measures *Plasmodium* species; sociodemographic details (including age, sex, and country of birth and residence); mortality; destination, duration, and purpose of international travel; and use of chemoprophylaxis.

Results Reported cases of imported malaria increased significantly over the 20 years of the study; an increasing proportion was attributable to *Plasmodium falciparum* (*P falciparum*/*P vivax* reporting ratio 1.3:1 in 1987-91 and 5.4:1 in 2002-6). *P vivax* reports declined from 3954 in 1987-91 to 1244 in 2002-6. Case fatality of reported *P falciparum* malaria did not change over this period (7.4 deaths per 1000 reported cases). Travellers visiting friends and relatives, usually in a country in Africa or Asia from which members of their family migrated, accounted for 13 215/20 488 (64.5%) of all malaria reported, and reports were geographically concentrated in areas where migrants from Africa and South Asia to the UK have settled. People travelling for this purpose were at significantly higher risk of malaria than other travellers and were less likely to report the use of any chemoprophylaxis (odds ratio of reported chemoprophylaxis use 0.23, 95% confidence interval 0.21 to 0.25).

Conclusions Despite the availability of highly effective preventive measures, the preventable burden from falciparum malaria has steadily increased in the UK while vivax malaria has decreased. Provision of targeted and appropriately delivered preventive messages and services for travellers from migrant families visiting friends and relatives should be a priority.

INTRODUCTION

Globally, malaria is estimated to affect 500 million people and to cause more than one million deaths a year.¹ Malaria acquired in endemic regions and imported into non-endemic countries accounts for a considerable and largely preventable burden of morbidity and mortality throughout Europe every year. Most general practitioners are involved in advising on prophylaxis against malaria, and most clinicians in the United Kingdom will be involved in diagnosing or treating cases of malaria. The increasing accessibility of international air travel and changing preferences for travel destinations mean that more people visit regions endemic for malaria, and they do so increasingly regularly.² Travellers to endemic areas can reduce their risk of malaria substantially by adopting preventive measures: avoiding mosquito bites and using appropriate chemoprophylaxis.³ Effective uptake of such measures is, however, largely dependent on the traveller's recognition and understanding of the risk. This in turn depends on an accurate risk assessment by healthcare workers who advise them; these risks change over time with shifts in the global epidemiology of malaria, changes in travel habits and patterns of migration (visits to friends and relatives are a common reason for travel), and changes in patterns of drug resistance.

We examined malaria notified in the UK in 1987 to 2006 inclusive, with the aim of identifying important trends and at risk groups to assist people advising travellers (mainly general practitioners) and those seeing unwell returned travellers (hospital doctors and general practitioners). We hypothesised that the group of travellers descended from migrant families visiting friends and relatives might be particularly at risk.

METHODS

The Malaria Reference Laboratory, part of the Health Protection Agency, provides reference and diagnostic parasitology services and maintains the national surveillance database of reported cases of malaria in the UK. Malaria surveillance is a passive detection

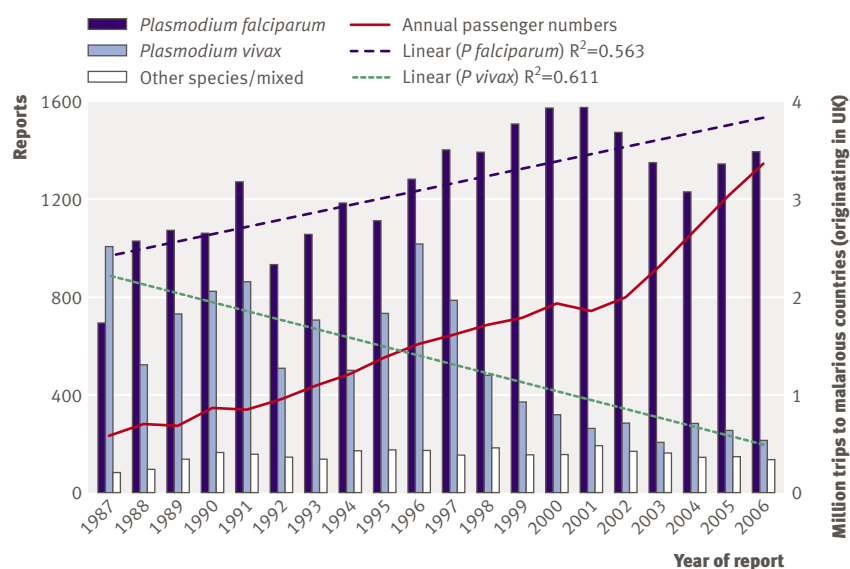


Fig 1 | Reported cases of malaria, 1987 to 2006

system that identifies cases from statutory notification (through local authorities) and from clinicians who send standardised malaria reports to the Malaria Reference Laboratory, usually accompanied by blood films for laboratory verification. Systems for case ascertainment for malaria in the UK are thought to be among the most effective in the world.⁴ Case definition, which remained identical over the period covered by this study, requires parasitological confirmation (blood films or tissue histology). Cases treated presumptively or solely reliant on alternative means of diagnosis (such as antigen tests) are not included. The notifying laboratory and clinician are requested to provide further information—personal details (date of birth, sex, country of birth, country of usual residence), details of travel (date of arrival in UK, country or region visited, purpose of travel, duration of travel), prophylaxis taken, and details of illness (date of onset, date of treatment, and method of diagnosis). Methods of case detection, reporting, and transcribing and the information requested from care providers used for this analysis remained unchanged between 1987 and 2006.

We included all reported episodes of malaria in the UK from 1 January 1987 to 31 December 2006 to provide 20

consecutive years. Supplementary information came from records of death certification for all malaria associated deaths and from records of postmortem findings where available. We entered data into dBase IV and used Microsoft Access 10 for cleaning and validation, including identification of duplicates and audit for transcription errors. Estimates of annual residential population denominators for England and Wales, Scotland, and Northern Ireland for the period 1987–2006 came from respective national statistical collections.^{5–7} Data on annual passenger numbers from the UK to individual “malarious countries” (as defined by the World Health Organization⁸), by purpose of travel, to selected countries in Africa and South Asia came from the international passenger survey for the years 1987 to 2006. This is a questionnaire based survey of a 0.2% stratified sample of travellers using British ports; detailed survey methods are described elsewhere.⁹ We did not analyse similar information for visitors to the UK.

We used Stata 10 for data analysis. We used Pearson’s χ^2 and Mantel-Haenszel methods for bivariate analysis of categorical variables, with Kruskal-Wallis test for equality of populations for comparison of non-normally distributed continuous variables. We used linear regression for analysis of linear trend. For bivariate analyses for which data were incomplete, we compared missing values with collected values. Where reported, confidence intervals are 95% and P values are two tailed.

RESULTS

Between 1987 and 2006, 39 300 cases of malaria were reported to the Malaria Reference Laboratory. Data were largely complete for central variables (age 96%, sex 94%, date of diagnosis 98%, outcome 99%) but less complete for some supplementary information (country of visit 88%, purpose of travel 71%, country of birth 64%, prophylaxis use 62%). The median age of cases was 31 years, and 38% were female. Malaria was attributable to a single species in 98.7% of cases: *P falciparum* 24 859 (63%) cases, *P vivax* 10 904 (28%), *P ovale* 6%, *P malariae* 1.5%, and one case of *P knowlesi*. Table 1 shows mortality by species and time period.

The pattern of malaria species has changed markedly over the study period. Reports of *P falciparum* increased through the study period (linear regression: $\beta=+27.4$ notifications/year, $P<0.0001$); increases for *P ovale* and

Table 1 | Reported cases of malaria and deaths from *Plasmodium falciparum* malaria, 1987–2006

Period	Reported malaria cases							Reported case rate, per million UK population				Deaths due to <i>P falciparum</i>	
	Pf	Pv	Po	Pm	Mixed	Species not confirmed	Total	Pf	Pv	Po	Pm	No	Case fatality (per 1000 cases)
1987–91	5 120	3 954	513	106	186	12	9 891	17.9	13.9	1.8	0.4	35	6.8
1992–6	5 546	3 475	638	152	169	1	9 981	19.2	12.0	2.2	0.5	41	7.4
1997–2001	7 440	2 231	675	160	80	6	10 592	25.4	7.6	2.3	0.6	59	7.9
2002–6	6 753	1 244	610	153	69	6	8 836*	22.5	4.2	2.0	0.5	48	7.1
Total	24 859	10 904	2 436	571	504	25	39 300	21.3	9.3	2.1	0.5	183	7.4

Pf=*Plasmodium falciparum*; Pm=*Plasmodium malariae*; Po=*Plasmodium ovale*; Pv=*Plasmodium vivax*.

*Includes one case of *P knowlesi*.

P. malariae were less pronounced. In contrast, reports of *P. vivax* declined over the study period (linear regression: $\beta = -36.2$ notifications/year, $P < 0.0001$) (fig 1). The ratio of *P. falciparum* to *P. vivax* infections increased from 1.3:1 in 1987-91 to 5.4:1 in 2002-6. Table 2 shows region of travel where malaria was acquired, by species; 96% of falciparum malaria was acquired in Africa, whereas 80% of vivax malaria came from South Asia.

Table 3 shows data on reason for travel. Where reason for travel was known, 20 488 cases, or 75% of imported cases, occurred in UK travellers (visitors from the UK to malarious countries); the remainder were among visitors to the UK. The number of journeys to malarious countries from the UK increased markedly (from 593 000 visits in 1987 to 2.6 million visits in 2004), but the median duration of visits to malarious areas of cases decreased (1987-91, 42 days; 1992-6, 35 days; 1997-2001, 28 days; 2002-6, 28 days). Of the UK travellers whose reason for travel was known, 13 215 (64.5%, 95% confidence interval 64% to 65%) had travelled to visit friends or relatives in their own or their families' country of origin. Most, but not all, of these people were visiting countries where their family had some degree of ethnic origin. The risk of malaria per episode of travel from the UK decreased between 1987 and 2006 for all species of malaria, most notably for *P. vivax* (fig 2).

Of the 34 359 cases with reported travel history, 24 599 (71.6%, 71% to 72%) occurred after travel to Africa; this included 20 774 of 21 541 (96.4%, 96% to 97%) cases of falciparum malaria. Sixty seven per cent of malaria in UK travellers arose after travel to west Africa; travel to Nigeria and Ghana accounted for 54% of all imported *P. falciparum*. Of those people who acquired malaria in west Africa, 76% were visiting friends or relatives in their own or their families' country of origin, whereas tourism was the most common purpose of travel for people visiting southern Africa (48%) and east Africa (44%). People who made trips to visit family in Africa were significantly more likely to have acquired malaria than those travelling for other reasons (risk ratio of reports per 10 000 trips = 3.65, 95% confidence interval 3.5 to 3.8; $P < 0.0001$).

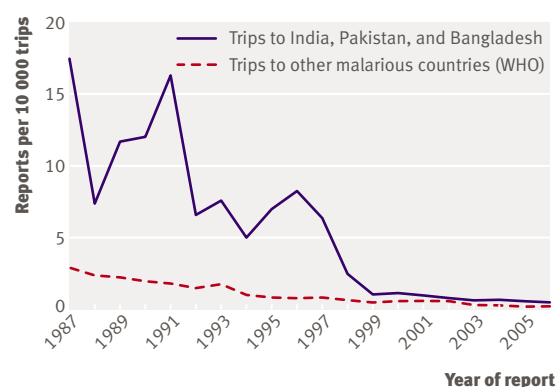


Fig 2 | Risk of reported *Plasmodium vivax* per travel episode to regions endemic for malaria

Travel to South Asia accounted for 8452 cases, 24.6%, (24% to 25%) of imported malaria, of which 92% was *P. vivax*. Over the study period, imported cases from this region declined significantly for all species of malaria despite a sustained increase in volume of travel. From 1987 to 1991, 3036 vivax cases arose from the Indian subcontinent, accounting for 31% of all UK malaria. By 2002-6, this had decreased to 705 cases (8% of all UK malaria). Of cases in which the purpose of travel was reported, 89% of UK travellers visiting South Asia had done so to visit family and friends. People travelling for this reason were at significantly higher risk of acquiring malaria than other travellers (risk ratio of reported cases per 10 000 trips = 7.9, 7.2 to 8.6; $\chi^2 P < 0.0001$).

Of UK travellers with complete records (17 129), only 42% reported taking any form of chemoprophylaxis against malaria during their period of travel. Significant differences existed in the use of chemoprophylaxis (including non-standard drugs) according to the geographical origin of cases (table 4), and people who had visited family in their country of origin were less likely to report the use of any prophylaxis than other travellers (Mantel-Haenszel odds ratio adjusted for age and sex = 0.23, 95% confidence interval 0.20 to 0.25). Among reported cases in people who travelled to sub-Saharan Africa between 1999 and 2006, over which period consistent recommendations on

Table 2 | Reported cases of malaria 1987-2006, by global region visited (where reported*). Values are numbers (percentages)

Region	<i>Plasmodium falciparum</i>	<i>Plasmodium vivax</i>	<i>Plasmodium ovale</i>	<i>Plasmodium malariae</i>	Total†
Africa	20 774 (96.4)	950 (9.7)	2 058 (98.0)	480 (98.0)	24 599
South Asia‡	517 (2.4)	7 813 (80.1)	23 (1.1)	3 (0.6)	8452
Far East and South East Asia	114 (0.5)	387 (4.0)	7 (0.3)	2 (0.4)	524
Central and South America	35 (0.2)	304 (3.1)	3 (0.1)	3 (0.6)	350
Oceania	46 (0.2)	263 (2.7)	7 (0.3)	1 (0.2)	333
Middle East	51 (0.2)	39 (0.4)	3 (0.1)	1 (0.2)	97
Caribbean	4 (0.01)	0	0	0	4
Total	21 541	9 756	2101	490	34 359

*Excludes 4927 reports with no travel information reported and 14 reports with no known history of travel.

†Includes one *P. knowlesi*, 455 mixed species, and 15 unconfirmed species reports.

‡Afghanistan, Burma (Myanmar), Bhutan, India, Pakistan, Bangladesh, Nepal, and Sri Lanka.

Table 3 | Purpose of travel among reported cases of malaria, 1987-2006 (where reported*)

	Median (interquartile range) duration of stay (days)	Cases	Deaths due to <i>Plasmodium falciparum</i>	Percentage (95% CI) cases reporting use of prophylaxis* (limited sample)
Travel originating in UK				
Travel originating outside UK				
Visiting family in country of origin	28 (21-58)	13 215	25	28.4 (27.5 to 29.2)
Holiday to malarious country	21 (14-56)	4 029	72	68.5 (67.0 to 70.0)
Business/professional travel	60 (21-168)	2 105	24	61.6 (59.4 to 63.8)
Foreign student in UK	28 (15-70)	548	0	NA
British armed forces	46 (28-110)	374	1	92.6 (89.1 to 95.1)
Children visiting parents living abroad	28 (21-42)	148	0	46.6 (37.9 to 55.4)
Civilian sea/air crew	14 (7-81)	69	2	43.6 (30.0 to 57.7)
Foreign visitor ill while in UK	28	3 331	15	NA
New entrant to UK	NA	2 602	3	NA
UK citizen living abroad	NA	1 010	15	46.8 (43.6 to 50.1)

NA=not applicable.

*Excludes 11 869 reports and 26 deaths for which purpose of travel was not stated or travel had not occurred.

prophylactic drugs for this region were made, only 7% of people visiting friends or relatives in their own or their families' country of origin reported having used recommended drugs, compared with 24% of people travelling for other reasons (χ^2 $P<0.0001$).

Probably reflecting the distribution of first generation and second generation immigrant groups, a striking geographical distribution of cases occurs in the UK (table 5). Forty one per cent of all cases of malaria in the UK, and 65% of cases of *P falciparum* malaria, occurred in London residents or visitors to London, whereas most (68%) cases of *P vivax* were reported from other regions of the UK, notably the West Midlands (a region encompassing the densely populated conurbations of Birmingham, Wolverhampton, Coventry, and Stoke-on-Trent). The seasonality of *P falciparum* cases shows a bimodal pattern, with peaks in January and September, mirroring patterns of travel to destinations where transmission of *P falciparum* occurs throughout the year (fig 3). By contrast, patterns of monthly *P vivax* reporting show a single summer peak, paralleling the peak transmission periods of malaria in much of India and Pakistan.

Mortality data show that 183 malaria related deaths occurred over the period of the study, giving an overall case fatality rate for *P falciparum* malaria of 7.4(95%

confidence interval 6.3 to 8.5) per 1000 cases; we found no evidence of a significant change over the period of study. Case fatality was significantly lower among people travelling from the UK to visit friends or relatives in their own or their families' country of origin than among people travelling for other reasons (0.25% *v* 1.9%; $\chi^2=83.1$, $P<0.001$).

DISCUSSION

This study of more than 39 000 cases of malaria imported into the UK shows striking trends. *P falciparum* malaria has increased steadily, which is a concern because these cases are potentially fatal; every year wholly preventable deaths do ensue in the UK. Reported cases are not distributed evenly across the population but are heavily concentrated in communities with frequent travel to see friends and relatives, especially in west Africa. Travellers to Nigeria and Ghana, neither of which is a common tourist destination, account for half of all imported falciparum cases. A minority of travellers with malaria report having used any prophylaxis, and much of that used is inadequate. Whereas falciparum is increasing, vivax malaria imported into the UK has dropped dramatically. Vivax malaria is also a disease of people visiting friends and relatives; in contrast to falciparum malaria, most cases are in people who reside outside London.

Disproportional burden of malaria in west African diaspora These data represent a public health failing but also an opportunity. They show that health messages are not getting through to ethnic minority groups visiting friends and relatives, especially in west Africa. Targeting messages tailored to these groups is essential in primary care and public health; this should be possible and would have a substantial impact on malaria in the UK. A halving of malaria in people in the African diaspora visiting friends and relatives would reduce malaria in UK travellers by almost a quarter. People visiting friends or

Table 4 | Use of chemoprophylaxis* among travellers from UK, by region of birth place

Region of birth	Cases	Prophylaxis taken	
		Yes	Percentage (95% CI)
Europe	5 674	3 493	61.6 (60 to 63)
Africa	5 914	1 699	28.7 (28 to 30)
South Asia	2 315	549	23.7 (22 to 26)
Other regions	387	223	57.6 (53 to 63)
Total	14 290	5 964	41.7 (41 to 42)

*Includes both recommended and non-standard drugs. Excludes 3359 case reports with no reported chemoprophylaxis information and 4285 with no birth place reported.

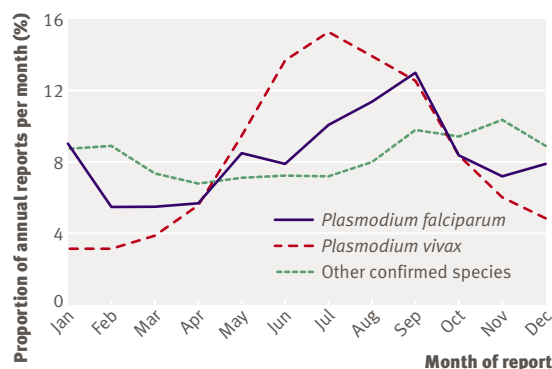


Fig 3 | Calendar month of onset of reported malaria in the UK, 1987 to 2006

relatives in their own or their families' country of origin may well expect to visit settings with a higher risk of transmission of malaria than other travellers and to do so for longer periods¹⁰⁻¹²; that many do this without the benefit of effective antimalarial chemoprophylaxis, as these and other data suggest,¹³⁻¹⁶ is of concern. Some evidence shows that people visiting friends or relatives in their own or their families' country of origin are less likely than tourists to self refer to travel health services before departure,¹⁷ are less likely to take up prophylaxis before they travel,¹⁸⁻²⁰ and adhere less to preventive measures while abroad.²¹ The personal cost of recommended chemoprophylaxis and fears of side effects have been suggested as direct disincentives that disproportionately affect high risk groups.²²⁻²³ However, little information is available on the cultural and ethnic basis of knowledge, attitudes, and practice regarding malaria and its prevention. Beliefs among adult travellers born in Africa that they remain protected from the severe consequences of malaria and that malaria is a trivial complaint have been reported.²⁴⁻²⁵

As the data reported here show, people of African origin do get malaria and indeed have a much higher risk of doing so than other travellers to Africa. Although these data are consistent with the findings of other studies that show travellers acquiring malaria on return to their country of origin to have a lower case fatality rate from malaria than other travelling groups,¹²⁻²⁶ deaths do occur.²⁷ Basing pre-travel advice on an assessment of the traveller's previous exposure to malaria cannot be justified, and falciparum malaria should always be managed as a preventable, potentially life threatening disease.³⁻²⁸

Disappearance of vivax cases imported from Asia

Whereas the increase in falciparum cases from Africa can be explained by increases in travel to highly endemic countries, changes in travel volume cannot explain the decline in vivax malaria. The synchronous decrease in *P. falciparum* notifications from India and Pakistan suggests that the decreases are not simply due to differential notification or hospital admission policies for cases caused by different malaria species but probably reflect a true reduction in the risk of exposure to malaria during travel. Annual prevalence reports for malaria over the same period have documented modest declines in South Asia (thought to have resulted from vigorous local control efforts, increasing urbanisation, and rising economic prosperity),⁸⁻²⁹ but nothing approaching the dramatic fall seen in cases imported to the UK and Europe.³⁰ One explanation might be that travellers visiting family in the region increasingly stay in urban settings where local control measures have been most effective in reducing local transmission of malaria. In the light of the reduction in the risk of imported malaria from South Asia, the risk-benefit assessment of the routine advice on chemoprophylaxis for the region may need to be re-examined, as has been the case for Latin

Table 5 | Reported malaria cases by UK region, 1987-2006*

UK region	Reported malaria cases					Reported cases per 1 000 000 population (mid-year estimates, 1987-2006)				
	Pf	Pv	Po	Pm	All species	Pf	Pv	Po	Pm	All species
England:										
South west	941	310	127	22	1 419	9.7	3.2	1.3	0.2	14.7
South east	3 107	1 287	354	85	4 896	19.8	8.2	2.3	0.5	31.2
East of England	1 553	813	172	30	2 604	14.7	7.7	1.6	0.3	24.7
West Midlands	716	2 263	71	9	3 091	6.8	21.5	0.7	0.1	29.3
East Midlands	378	451	48	12	906	4.6	5.5	0.6	0.1	11.0
Yorkshire and the Humber	554	1 003	74	14	1 661	5.6	10.1	0.7	0.1	16.7
North west	300	538	21	8	878	2.2	3.9	0.2	0.1	6.4
North east	115	60	11	1	190	2.2	1.2	0.2	0.02	3.7
London	15 843	3 463	1 380	355	21 345	112.1	24.5	9.8	2.5	151.0
Wales	252	118	38	8	423	4.4	2.0	0.7	0.1	7.3
Scotland	480	338	67	15	913	4.7	3.3	0.7	0.1	9.0
N Ireland	73	37	9	1	120	2.2	1.1	0.3	0.03	3.6
Total	24 312	10 681	2 372	560	38 446	20.8	9.1	2.0	0.4	32.9

Pf=Plasmodium falciparum; Pm=Plasmodium malariae; Po=Plasmodium ovale; Pv=Plasmodium vivax.

*Excludes 854 cases with missing postcode.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Falciparum malaria is the most common potentially fatal tropical parasitic infection imported into the UK

Increased travel to areas endemic for malaria means that increasing numbers of UK residents are at risk

Effective prophylactic and anti-mosquito measures are available

WHAT THIS STUDY ADDS

Imported falciparum malaria has been increasing over the past 20 years, but vivax malaria has been decreasing markedly

Most malaria is in travellers visiting friends and relatives in their families' country of origin, especially in west Africa

Uptake of chemoprophylaxis is low in people who acquire malaria, especially travellers from migrant families, and tailoring health messages to migrant groups is a priority

America.³¹ Nevertheless, cases of malaria continue to occur and travellers need to be warned to have any fever investigated rapidly for malaria.

Limitations of study

The advantages of large scale, prospectively collected data from surveillance centres collected in an unchanged, standardised way over long periods are clear, but limitations also exist. Under-reporting is inevitable,³² and laboratories and clinicians differ in the comprehensiveness of their reporting. Previous studies of data from the Malaria Reference Laboratory suggest that they are more complete than most other routinely collected data on malaria and are in excess of 50% complete.⁴ Nevertheless, the true burden of malaria in the UK is almost certainly higher than these surveillance results suggest. As the methods did not change over this period, however, this is unlikely to affect trends reported here, particularly the relative increase in one species and decline in another seen in this study, or to explain the heavy concentration of cases in people visiting friends and relatives. Reporting clinicians often did not report information about travel history and prophylaxis, but we found no evidence to suggest that cases with missing information were systematically different from those with complete reports. Even when information about preventive measures is requested of travellers, adherence to such measures may be difficult to assess.

Implications of findings

This study highlights the need for general practitioners and people involved in public health to focus tailored messages on preventing malaria on members and descendants of migrant families visiting friends and relatives, especially in African migrant families. The UK has guidelines based on consensus that highlight the need for all UK residents, irrespective of country of birth, to use effective antimalarial prophylaxis when visiting highly endemic areas.³³ Changes to public health policy, including the current policy of charging for antimalarial prophylaxis, may need to be considered. Malaria is an almost entirely preventable, potentially fatal, disease that poses a considerable risk to some migrant groups.

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