11 Meer B, Baker JA. The Stockton geriatric rating scale. *J Gerontol* 1966;**21**:392-403.
12 Mac Nair DM, Kahn RJ. Self assessment of cognitive deficits. In: Crook T, Ferris S, Bartus R, eds. *Assessment in geriatric psychopharmacology*. New Canaan, Conn: Marc Powley, 1983:137-44.
13 Marx JL. Alzheimer's drug trial put on hold. *Science* 1987;**238**:1041-2.
14 Hills M, Armitage P. The two-period cross-over clinical trial. *Br J Clin Pharmacol* 1979;**8**:7-20.
15 SAS Institute. *SAS user's guide: statistics, version 5*. Cary, NC: SAS Institute, 1985.
16 Kaye WH, Sitaram N, Weingartner H. Modest facilitation of memory in dementia with combined lecithin and anticholinesterase treatment. *Biol Psychiatry* 1982;**17**:275-80.
17 Gauthier S, Masson H, Gauthier L, *et al*. Tetrahydroaminoacridine and lecithin in Alzheimer's disease. In: Giacobini E, Becker R, eds. *Current research in Alzheimer therapy*. London: Taylor and Francis, 1988:237-45.
18 Little A, Levy R, Chuaqui-Kidd P, Hand D. A double-blind placebo-controlled trial of high-dose lecithin in Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 1985;**48**:736-42.
19 Perry EK, Tomlinson BE, Blessed G, *et al*. Correlation of cholinergic abnormalities with senile plaques and mental scores in senile dementia. *Br Med J* 1978;ii:1457-9.
20 Pocock SJ, Hughes MD, Lee RJ. Statistical problems in the reporting of clinical trials. A survey of three medical journals. *N Engl J Med* 1987;**317**:426-32.
21 Penn RD, Martin EM, Wilson RS, Fox JH, Savoy SM. Intraventricular bethanechol infusion for Alzheimer's disease: results of a double-blind and escalating-dose trial. *Neurology* 1988;**38**:219-22.
22 Ames DJ, Bhatal PS, Davies BM, Fraser JRE. Hepatotoxicity of tetrahydroacridine. *Lancet* 1988;i:887.
23 Wilcock GK, Surmon D, Forsyth D, Morgan R. Cholinergic side-effects of tetrahydroaminoacridine. *Lancet* 1988;ii:1305.

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Risk of malaria in British residents returning from malarious areas

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Abstract

***Objectives*—To identify which British residents travelling abroad are at greatest risk of malaria infection, and to determine the efficacy of malaria chemoprophylaxis for preventing *P falciparum* infections in tropical Africa.**

***Design*—Prospective cohort study (case-base linkage) with routine national surveillance systems. Denominators (base population) were obtained from monitoring a random sample of returning British travellers with the international passenger survey. Numerators (cases) were obtained from reports of malaria infections in British residents, through the Malaria Reference Laboratory network.**

***Setting*—International passenger survey conducted at passport control of international airports in Britain. Malaria reports received nationally were collated centrally in London.**

***Subjects*—2948 British residents (0·2%) returning to Britain in 1987 randomly selected and questioned and 1052 British residents with microscopically confirmed malaria infections in 1987, whose case reports were reviewed and on whom additional data were collected by postal survey.**

***Main outcome measures*—Annual incidence subdivided by categories of risk. Chemoprophylactic efficacy for east and west Africa by principal regimens and compliance.**

***Results*—Annual rates of reported infection per 100 000 travellers to Oceania were 4100; to west and east Africa were 375 and 172 respectively; to Latin America, the Far East, and the Middle East were 12, 2, and 1 respectively. Immigrants visiting friends and relatives in Ghana and Nigeria were at greatest risk (1303 and 952 per 100 000 respectively) in west Africa. Business travellers to Kenya experienced the highest attack rates in east Africa (465 per 100 000). Age-sex specific attack rates varied by region. No prophylaxis was reported to have been used by 23% of British visitors to west Africa, 17% to east Africa, 46% to central or southern Africa, and 58% visiting south Asia. The efficacy of chloroquine plus proguanil against *P falciparum* infection was 73% and 54% in west and east Africa respectively. Lower values were obtained for chloroquine alone and proguanil alone. The efficacy of Maloprim (pyrimethamine-dapsone) was 61% in west Africa, but only 9% in east Africa. Visitors to west Africa who did not comply with their chemoprophylactic regimen were at a 2·5-fold higher risk of infection than fully compliant users. Non-compliant visitors to east Africa had similar rates of infection as non-drug users.**

***Conclusions*—In 1987 chloroquine plus proguanil was the preferred chemoprophylactic regimen for *P falciparum* infection in Africa; antimalarial drugs must be taken regularly to be effective.**

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Introduction

The control of malaria in semi-immune indigenous communities has become increasingly difficult with the spread of chloroquine resistant strains of *Plasmodium falciparum*.[1] There are also serious public health implications for international travellers, most of whom have no protective immunity against malaria. The reported incidence of *P falciparum* infections in Britain has risen sharply in recent years with over 1000 cases recorded by the Malaria Reference Laboratory in 1988.[2] The trend can be expected to continue as more travellers visit areas where the degree and intensity of transmission of resistant strains of *P falciparum* will also increase. Protection against infection in areas with a high transmission of *P falciparum* parasites has become a particular problem. Though some drugs—namely, pyrimethamine-dapsone (Maloprim), pyrimethamine-sulphadoxine (Fansidar), and amodiaquine—have offered greater protection against infection than chloroquine or proguanil, the risk of serious adverse reactions associated with their use has been considered to be unacceptable in otherwise healthy subjects, unless the risk of a potentially fatal infection is high.[3,4] Chloroquine plus proguanil has thus been the principal regimen advised for British travellers visiting areas of sub-Saharan Africa, the origin of over 80% of *P falciparum* infections imported into Britain.[5] It is not known, however, how much protection this regimen now offers non-immune visitors exposed to *P falciparum* infections. Early formulation of this regimen originated from one retrospective cohort study conducted between 1978 and 1983, which illustrated empirically that 200 mg of proguanil daily, alone and combined with chloroquine, was a highly effective regimen in east Africa.[6] Although more recent prospective cohort studies have been performed, efficacy data generated from these studies have not been adequate to guide current recommendations.[7-9] The limitations of such cohort studies are now well recognised; they can be expected to provide data on efficacy only for select populations at very high risk of malaria (above 1%), if drug prophylaxis is controlled, and when the diagnoses are verified microscopically.[10] Data on the risk of infection with malaria in different subgroups and the relative efficacy of chemoprophylactic regimens under varying epidemiological conditions are, however, required to ensure that recommendations for chemo-

prophylactic drugs are targeted appropriately. Alternative methods of obtaining such data must thus be sought and we describe one method, case-base linkage, here. We used data generated from national surveillance systems to measure the rates of infection in returning British residents in 1987, the efficacy of commonly prescribed chemoprophylactic regimens for travellers visiting east and west Africa, and the influence of poor compliance on the protective value of these regimens.

Subjects and methods

CASE AND BASE POPULATION

Malaria cases—All of the 1816 microscopically confirmed cases of malaria in Britain reported to the Malaria Reference Laboratory during 1987 were investigated. Of these, 1052 patients were British residents, broadly defined as any person resident in the United Kingdom prior to travel. These patients were followed up individually to verify reported surveillance data and to collect additional data missing from the routine report forms.[11]

Data on travel in the base population were derived from a continuous monitoring system, the international passenger survey, designed and implemented by the Office of Population Censuses and Surveys, and from the Department of Employment. The survey methods have been reported in full elsewhere.[12] Briefly, a 0·2% stratified sample of returning British travellers was questioned on entering Britain by trained interviewers with a standard questionnaire. Throughout the study year, in addition to routine questions, 2948 sampled British residents visiting malarious areas were questioned on their use of, and compliance with, recommended chemoprophylactic drug regimens. The total number of returning British residents visiting malarious areas was calculated to be 1·6 million. This was estimated by assigning weights to each sampled traveller, allotted by the Office of Population Censuses and Surveys according to the sampling interval and shift rota operating at the time of incoming flights. Analyses were conducted using the statistical package for the social sciences (SPSS X).

CASE-BASE LINKAGE

Analyses of rates of infection—Measurements of rates of infection and the efficacy of drugs were achieved by linking together information on cases in reports of the Malaria Reference Laboratory with that on the base population (from international passenger survey travel statistics) as if both were derived from one single study population. The travel category of patients was adjusted to concur with international passenger survey definitions; tourists were grouped under holiday travellers; business, crew, military, and expatriate patients were redefined as business travellers; and those remaining cases travelling for family reasons (including overseas students receiving education in Britain) were reclassified as visiting friends or relatives. Case and base data were then aggregated to compute species-specific malaria attack rates per 100 000 visits to each region and the principal countries of visit. Regional malaria attack rates were calculated according to the purpose of visit of British travellers, their age and sex, and their duration of stay abroad. Two tailed standard normal deviates were used to test significance.

Measurement of chemoprophylactic efficacy—Information on the use of chemoprophylaxis by British patients with malaria was derived first from case report forms and then verified by following up individual patients. Information obtained from the sampled travellers collected during the international passenger survey study was used to estimate the proportion of all travellers using each chemoprophylactic regimen. These were stratified according to the region of visit and category of traveller. No data on blood drug concentrations were available to verify the reported use of chemoprophylaxis. Malaria attack rates, relative risks, and chemoprophylactic efficacy were calculated to measure the protective effect of commonly prescribed chemoprophylactic drugs against *P falciparum* infections in British travellers visiting east and west Africa in 1987. Malaria attack rates indicated the incidence of infection per 100 000 travellers for each chemoprophylactic regimen. Relative risk was calculated to describe the risk of infection in travellers taking no drugs compared with that in travellers taking chemoprophylaxis. Chemoprophylactic efficacy was estimated using the conventional formula; $CPE_i = (R^nCP - RCP_i)/R^nCP \times 100$ (where CPE_i equals the percentage reduction in risk attributed to chemoprophylaxis with CP_i compared with similarly exposed travellers taking no chemoprophylaxis (^nCP); R^nCP is the risk of infection in travellers to a specified region without chemoprophylaxis; and RCP_i is the risk of infection in travellers using CP_i). Calculation of 95% confidence intervals of the relative risk was by Mietinens test-based approximation, using the square root of the χ^2 significance value[13]; 95% confidence interval = relative risk$^{(1 \pm 1 \cdot 96/x)}$ and 95% confidence intervals for efficacy were derived from the upper and lower 95% confidence interval units of the relative risk; relative risk − 1/relative risk. Efficacy values and relative risks were then calculated according to the reported compliance, with full compliance defined as the uninterrupted use of chemoprophylactic drugs taken, as prescribed, on the allocated day.

Results

MALARIA ATTACK RATES

Reported species-specific attack rates by region of infection—British residents visiting Oceania were at the highest risk of malaria infections; 4% of them were infected on their return to Britain (table I), mainly with *P vivax* infection acquired during expeditions in Papua New Guinea. Of those visiting sub-Saharan Africa, travellers to west Africa were at greatest risk of *P*

TABLE I—*Regional malaria attack rates (per 100 000) by species of parasite in returning British residents, 1987*

Region and principal countries	No of travellers (000s)*	Reported cases (attack rates)		
		All species	*P falciparum*	*P vivax*
		West Africa		
Total	75·7	287 (379)	246 (325)	12 (16)
Nigeria	26·5	147 (555)	128 (483)	5 (19)
Ghana	9·5	74 (779)	66 (695)	2 (21)
Gambia	25·4	7 (28)	5 (20)	1 (4)
		East Africa		
Total	63·3	109 (172)	73 (115)	27 (43)
Kenya	49·0	73 (149)	54 (110)	13 (27)
Tanzania	6·6	14 (212)	10 (151)	4 (61)
		Central or southern Africa		
Total	40·6	52 (128)	42 (103)	6 (15)
Zambia	14·5	20 (138)	16 (110)	2 (14)
Malawi	1·9	15 (789)	14 (737)	1 (53)
		South Asia		
Total	297·2	525 (177)	18 (6)	497 (167)
India	156·4	354 (226)	10 (6)	339 (217)
Pakistan	98·6	164 (166)	5 (5)	155 (157)
		Oceania		
	1·0	41 (4100)	3 (300)	37 (3700)
		Far East or South East Asia		
Total	306·4	7 (2)	2 (<1)	5 (2)
Thailand	45·7	3 (7)	2 (4)	1 (2)
		Latin America		
	57·1	7 (12)	1 (2)	6 (11)
		Middle East		
	201·0	3 (1)	1 (<1)	2 (1)
		Other		
	565·7	21	10	9
Total	1608·0	1052 (65)	396 (25)	601 (37)

*Estimated from international passenger survey sample survey.

TABLE II—*Malaria attack rates (per 100 000) by purpose of travel in British travellers, 1987*

Region and principal countries	Tourist			Business			Visiting friends or relatives		
	No of cases	No of travellers* (000s)	Rate	No of cases	No of travellers* (000s)	Rate	No of cases	No of travellers* (000)	Rate
				West Africa					
Total	38	34·5	110	71	23·7	300	152	15·6	974
Nigeria	9	5·3	170	25	8·8	284	100	10·5	952
Ghana	9	1·3	692	18	4·9	367	43	3·3	1303
Gambia	4	22·1	18	2	2·2	91	1	1·0	100
				East Africa					
Total	33	36·7	90	46	11·6	397	19	12·4	153
Kenya	26	32·6	80	27	5·8	466	8	9·4	85
Tanzania	4	2·3	174	3	1·3	231	6	2·5	240
				Central or southern Africa					
Total	17	15·2	112	22	12·7	173	6	12·3	49
Zambia	4	7·25	55	9	5·25	171	2	2·0	100
Malawi	5	1·0	500	4	—		4	0·9	444
				South Asia					
Total	48	105·4	46	12	28·4	42	420	153·3	274
India	33	62·6	53	8	17·8	45	284	70·0	405
Pakistan	15	23·9	63	2	6·0	33	132	65·4	202
				Far East or South East					
	3	140·5	2	3	106·7	3	1	51·5	2
				Oceania					
	11	—		20	1·0	2000	4	—	
				Middle East					
	1	79·0	1	2	40·8	5	0	59·1	0
				Latin America					
	4	26·0	15	3	22·9	13	0	6·2	0

*Estimated from international passenger survey. — = not included in international passenger survey.

TABLE III—*Malaria attack rates (per 100 000) in British travellers by age and sex, 1987*

Age (years)*	West Africa				East Africa				Central or Southern Africa				South Asia			
	Male	Female	Rate risk in males†	p Value‡	Male	Female	Rate risk in males†	p Value‡	Male	Female	Rate risk in males†	p Value‡	Male	Female	Rate risk in males	p Value‡
0-·15	658	248	2·7	0·003	141	—	—	—	90	67	1·3	0·7	210	174	1·2	0·317
16-24	532	229	2·3	0·005	560	141	4·0	0·0002	437	67	6·5	0·0007	208	198	1·1	0·97
25-34	504	412	1·2	0·37	256	104	2·5	0·02	420	540	[1·3]	0·6	129	137	[1·1]	0·74
35-54	282	343	[1·2]	0·42	120	99	1·2	0·68	180	288	[1·6]	0·27	118	167	[1·4]	0·036
55-64	147	229	[1·6]	0·48	106	82	1·3	0·7	360	36	10·0	0·0083	221	212	1·0	0·96
≥65	172	—	—	—	369	164	2·3	0·36	—	—	—	—	387	479	[1·2]	0·55
All	372	265	1·4	0·19	221	94	2·3	0·0001	237	130	1·8	0·017	160	178	[1·1]	0·23

— Inadequate data.
*Intervals according to international passenger survey.
†Compared with females becoming infected (reciprocal values [ ] when rate risk <1).
‡Derived from two tailed standard normal deviates.

falciparum infections, particularly in Ghana, where the rate approached 1% per visit. Malaria attack rates for travellers returning from south Asia were low; the *P vivax* specific attack rate for this region was 167 per 100 000 travellers. Rates of infection in British residents returning from the Far East or South East Asia, South America, and the Middle East were very low, with 2, 12, and 1 infection per 100 000 respectively.

Reported regional attack rates by purpose of travel—Malaria attack rates were usually highest in British residents travelling to malarious areas to visit friends or relatives (table II). Travellers to west Africa and south Asia constitute immigrant groups resident in Britain. The rates approached 1% in these visitors to west Africa and were higher than 1% in travellers returning from Ghana. The rates in travellers from west Africa were 6·4 times greater than the rate in those visiting friends or relatives in east Africa. Business travellers returning from east Africa, principally Kenya, were at greater risk than tourists and those visiting friends or relatives. Tourists visiting Kenya were, however, at 4·4-fold higher risk of infection compared with those visiting the Gambia.

Reported age and sex specific attack rates by region of infection—Males had a significantly higher malaria attack rate than females visiting sub-Saharan Africa (table III). Males aged between 16 and 24 returning from east Africa had a fourfold higher risk of infection compared with females of the same age, and in those returning from central or southern Africa the difference was more than sixfold higher. Boys (0-15 years) visiting west Africa had a 2·7-fold higher risk of infection than girls of the same age. Rates between males and females did not differ significantly in travellers to south Asia but were highest in travellers aged over 65.

Reported rates according to duration of travel—Malaria attack rates did not always increase proportionately with the length of time abroad (table IV). The relative risk of infection in west Africa increased from 1·0 for one week to 80·3 when trips lasted between six months and a year. Remarkably, travellers visiting east Africa for one week were at fivefold greater risk than those abroad for one month.

PROTECTION AFFORDED BY MALARIA CHEMOPROPHYLAXIS

Types of chemoprophylactic drug taken by British travellers

No chemoprophylactic drugs were reportedly taken by 23% of travellers to west Africa, 17% of those to east Africa, 46% to central or southern Africa, and 58% to south Asia (table V). The recommended drug regimen for sub-Saharan Africa, chloroquine plus proguanil, was reportedly used by nearly half of British residents travelling to east Africa for business or on holiday and to west Africa on holiday. A fifth of holiday travellers to east Africa and to central or southern Africa used Maloprim, alone or with proguanil or chloroquine. Drugs not currently recommended (pyrimethamine, amodiaquine, and Fansidar) were used by a small proportion of all groups.

Regional efficacy of commonly prescribed chemoprophylactic drugs

West Africa—Travellers to west Africa taking no chemoprophylaxis were at a threefold higher risk of becoming infected with *P falciparum* than those taking chloroquine plus proguanil (table VI). The calculated efficacy of each commonly prescribed regimen was over 50%, but the confidence intervals were wider with chloroquine and Maloprim. Chloroquine plus proguanil had the highest efficacy at 73% with narrow confidence intervals. Proguanil alone seemed to give greater protection than chloroquine alone.

East Africa—The *P falciparum* attack rate in travellers taking no chemoprophylaxis in east Africa was 196 per 100 000. Although this was 3·5 times lower than for travellers taking no chemoprophylactic in west Africa, the efficacy of each drug was lower in east than west Africa (table II). The efficacy of chloroquine and chloroquine plus proguanil was 54% and that of proguanil was 36%. The confidence intervals were wide for each regimen with the lower limits falling below 0%. Maloprim (alone or, rarely, in combination with proguanil or chloroquine) had a very low efficacy (9%).

Compliance with chemoprophylaxis

Poor compliance with prophylaxis compromised the protective value of all drugs (table VII). Among travellers returning from west Africa those who were non-compliant had a 2·5-fold higher rate of infection with *P falciparum* than those reporting full compliance. Poorly compliant users did, however, seem to be protected still, especially with drugs taken daily rather than weekly, although the lower confidence limits for drug efficacy dropped to below 0%. Everyone taking Maloprim reported full compliance. Chloroquine and chloroquine plus proguanil seemed to be as effective in east Africa as in west Africa but only in fully compliant users. The confidence intervals for drug efficacy for east Africa were, however, very wide, with lower limits below 0% for all drug regimens except chloroquine plus proguanil, and the efficacy was not significantly different. Drugs taken by non-compliant users in east

TABLE IV—*Malaria attack rates (per 100 000) and relative risk of infection in British travellers by duration of travel**

Duration of travel (weeks)	West Africa				East Africa			
	No of cases	No of travellers	Rate	Relative risk*	No of cases	No of travellers	Rate	Relative risk†
1	9	14 721	61	1·0	6	2 752	218	1·0
2	19	22 387	85	1·4	8	11 693	68	[3·2]
3	26	9 192	283	4·6	14	19 198	73	[3·0]
4	74	14 472	511	8·4	6	14 897	40	[5·5]
5-12	68	12 334	551	9·0	34	8 938	380	1·7
13-26	13	347	3746	61·4	11	2 502	440	2·0
27-52	17	347	4899	80·3	14	720	1944	8·9

*Excludes cases and travellers whose stay was longer than one year.
†Compared with risk from one week's travel ([] denotes reciprocal value).

TABLE V—*Proportion (%) of British travellers reportedly using malaria chemoprophylactic drugs and purpose of travel, 1987*

	West Africa				East Africa				Central or Southern Africa				South Asia			
	Total	Holiday	Business	Visiting friends and relations	Total	Holiday	Business	Visiting friends and relations	Total	Holiday	Business	Visiting friends and relations	Total	Holiday	Business	Visiting friends and relations
None	23	17	14	46	17	11	21	30	46	32	60	48	58	45	50	69
Chloroquine	14	15	14	14	11	10	4	21	3	5	0	4	11	12	8	9
Proguanil	15	10	21	16	8	10	4	6	7	5	13	4	8	12	7	5
Chloroquine and proguanil	30	44	21	11	42	45	46	27	23	32	20	16	12	20	25	5
Maloprim	4	2	11	0	16	20	13	9	14	21	7	12	6	7	7	5
Pyrimethamine	9	7	14	5	2	1	8	<1	3	5	0	4	4	3	2	5
Amodiaquine	3	2	4	5	4	3	4	6	4	0	0	12	<1	0	<1	1
Fansidar	2	2	<1	3	0	0	0	0	0	0	0	0	<1	<1	0	<1

TABLE VI—*Universal efficacy* of chemoprophylactic drugs against P falciparum used by British travellers 1987*

	West Africa			East Africa		
	Malaria attack rate (per 100 000)	Relative risk*	Chemoprophylactic efficacy† (95% confidence interval)	Malaria attack rate (per 100 000)	Relative risk*	Chemoprophylactic efficacy† (95% confidence interval)
			Unadjusted for compliance			
Chloroquine	275	2·5	60 (40 to 73)	90	2·2	54 (−52 to 86)
Proguanil	219	3·1	68 (51 to 79)	126	1·6	36 (−167 to 85)
Chloroquine and proguanil	183	3·7	73 (62 to 81)	91	2·2	54 (−5 to 79)
Maloprim	266	2·6	61 (23 to 80)	178	1·1	9 (−449 to 98)
Other	142			81		
None	681			196		
			Adjusted for full compliance			
Chloroquine	230	3·0	66 (47 to 79)	68	2·9	65 (−26 to 90)
Proguanil	155	4·4	77 (61 to 87)	126	1·6	36 (−167 to 85)
Chloroquine and proguanil	150	7·8	78 (68 to 85)	50	3·9	75 (38 to 89)
Maloprim	266	2·6	61 (23 to 80)	161	1·2	18 (−267 to 82)

*No chemoprophylaxis *v* specified regimens. †Percentage reduction in risk of infection attributed to chemoprophylaxis.

TABLE VII—*Influence of compliance on efficacy of chemoprophylactic drugs against P falciparum, 1987*

	West Africa						East Africa					
	Compliance		Non-compliance				Compliance		Non-compliance			
	Rate of infection	Chemoprophylactic efficacy†	Rate of infection	Chemoprophylactic efficacy†	Relative risk*	p Value	Rate of infection	Chemoprophylactic efficacy†	Rate of infection	Chemoprophylactic efficacy†	Relative risk*	p Value
Chloroquine	230	66	571	16	2·5	0·023	68	65	272	<1	4·0	0·081
Proguanil	155	77	372	45	2·4	0·026	126	36	—			
Chloroquine and proguanil	150	78	370	46	2·5	0·0067	50	75	245	<1	5·0	<0·0001
Maloprim	266	61	—				161	18	282	<1	1·8	0·317

—Inadequate data for analyses. *Compliance *v* non-compliance. †Percentage reduction in risk of infection attributed to chemoprophylaxis.

Africa did not seem to offer any protection against *P falciparum* infection.

Discussion

We have described a method for collecting and measuring the national risk of malaria in British residents returning from malarious areas. Although multiple analyses were not possible, the data indicated significant differences in risk between the various groups of travellers. Former crude analyses of data suggested that immigrant groups and young males were at greatest risk,[5] and our present data support such findings. Rates of infection with *P falciparum* in travellers returning from west Africa were particularly high and were double those of 1986. A further rise in incidence has since been reported, in 1988.[2] Transmission in Ghana was especially high. In contrast, rates of infection from south Asia have dropped in recent years and seem to mirror a lull in transmission from this region, but this is thought to be temporary as a sharp rise in *P vivax* malaria has been reported during 1989. High infection rates in immigrant groups from west Africa cannot be blamed solely on the absence of chemoprophylaxis: though prophylaxis has been shown to reduce attack rates by a half, the rates of infection in immigrants taking chemoprophylaxis still remained in the order of 0·7%. Infection rates in travellers to east Africa were not as high as expected; business travellers seemed to be at greatest risk, and this group contributed towards the disproportionately high attack rate in British residents abroad for only one week. Rates in longer term travellers, including those visiting relatives or friends, were lower, possibly because many of these travellers were based in Nairobi.

Incidence data alone have previously implied that males, particularly children and young adults, were at greater risk than females.[5] This was assumed to be partly because more males than females visited high risk malarious areas. Our data suggest that males do seem to have a higher risk of infection than females visiting the same regions. This may relate to an increased exposure to infection or decreased protection, or both. An equal proportion of males and females, however, reported taking chemoprophylaxis, and the duration of stay abroad did not differ significantly between males and females.[14] Further analyses on compliance with prophylaxis indicated that males were less compliant than females in each age category and that younger travellers were less compliant than older travellers, which has been reported previously.[5] We thus conclude that an important reason for the excess risk in males is because of their decreased compliance with prophylaxis.

The efficacy of commonly prescribed chemoprophylactic drugs was calculated on a regional basis. Resistance of *P falciparum* to chloroquine and alternative antimalarial drugs varies geographically, even by microlocation. Such precision was not possible using routine surveillance data, which were not adequate to measure efficacy for individual countries. However, as recommendations for chemoprophylaxis are generally made regionally, and year by year the proportion of travellers visiting each country within a region varies only marginally,[12] efficacy within regions was considered to be of some value. Firstly, the mean values, when read together with their confidence intervals, illustrated that drugs had a higher protective value in west Africa than in east Africa. Secondly, the data indicated that monoprophylaxis offered less protection, particularly for proguanil alone and for Maloprim in travellers to east Africa. Chloroquine plus proguanil is thus the preferred regimen for Africa. Thirdly, and of great importance, the data measured the decreased value of prophylaxis if drugs were not taken on a regular basis. The protective effect of drugs was particularly low in poorly compliant travellers to east Africa.

The incidence of *P falciparum* infections has increased since this study were performed; it is thought that the protective value of chloroquine plus proguanil has fallen. New drugs to which strains of *P falciparum* are sensitive have been developed and will shortly be available in Britain. Past experience of toxicity associated with newer, more potent drugs, however, illustrates the need for caution in prescribing drugs too widely.[3,4] One drug, mefloquine, has been recommended for prophylaxis against multiresistant strains of *P falciparum* malaria.[15] Its use will be restricted to travellers abroad for short periods because it has a particularly long half life, and longer term use may cause problems with the dosing schedule. Our data illustrate, however, that it is long term rather than short term travellers who will be most in need of a new drug.

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1 World Health Organisation. The epidemiology of drug resistant malaria parasites: memorandum from a WHO meeting. *Bull WHO* 1987;**65**:797-816.
2 Bradley DJ. Current trends in malaria in Britain. *J R Soc Med* 1989;**82**(Suppl 17):8-14.
3 Peto TEA, Gilks CF. Strategies for the prevention of malaria in travellers: comparison of drug regimens by means of risk benefit analysis. *Lancet* 1986;ii:1256-60.
4 Phillips-Howard PA, West L. Serious adverse drug reactions to pyrimethamine-sulphadoxine, pyrimethamine-dapsone, and to amodiaquine in Britain. *J R Soc Med* (in press).
5 Phillips-Howard PA, Bradley DJ, Blaze M, Hurn M. Malaria in Britain: 1977-1986. *Br Med J* 1988;**296**:245-8.
6 McLarty DG, Webber R, Jaatinen M, *et al*. Chemoprophylaxis of malaria in non-immune residents in Dar es Salaam, Tanzania. *Lancet* 1984;ii:656-9.
7 Lobel HO, Phillips-Howard PA, Brandling-Bennett AD, *et al*. Malaria incidence and prevention among European and North American travellers to Kenya. *Bull WHO* (in press).
8 Fogh S, Schapira A, Bygbjerg IC, *et al*. Malaria chemoprophylaxis in travellers to east Africa: a comparative prospective study of chloroquine plus proguanil with chloroquine plus sulfadoxine-pyrimethamine. *Br Med J* 1988;**296**:820-2.
9 Harries AD, Foreshaw CJ, Friend HM. Malaria prophylaxis amongst British residents of Lilongwe and Kasungu districts, Malawi. *Trans R Soc Trop Med Hyg* 1988;**82**:690-2.
10 Phillips-Howard PA. Efficacy of drug prophylaxis. *J R Soc Med* 1989;**82** (Suppl 17):18-30.
11 Phillips-Howard PA, Mitchell J, Bradley DJ. Validation of malaria surveillance reports: implications for studies of malaria risk. *J Epidemiol Community Health* (in press).
12 Phillips-Howard PA, Breeze E, Lakin C, Bradley DJ. Short term travel to malarious areas; malaria risk in UK travellers. *Travel Medicine International* 1988;**6**:51-60.
13 Kirkwood B. *Essentials of medical statistics*. Oxford: Blackwell Scientific Publications, 1988:174-5.
14 Phillips-Howard PA. The epidemiology of malaria in Britain [PhD thesis]. London: University of London, 1988. 366 pp.
15 Prophylaxis against malaria for travellers from the United Kingdom. *Br Med J* 1989;**299**:1087-9.

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