

**Compliance and reported adverse
effects of malaria chemoprophylaxis
among travelers: a prospective study
(Preliminary Result)**

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Outline

- Background
- Objective
- Method
- Result
- Conclusion

Background

- Malaria is the most common diagnosis of fever in returned travelers ¹
- It accounted for 33% of deaths among febrile travelers ¹
- The most important method to prevent malaria is mosquitoes prevention

1. Wilson ME, et al. **Fever in Returned Travelers: Results from the GeoSentinel Surveillance Network.** *Clinical Infectious Diseases* 2007;44:2560-68

Background

- Chemoprophylaxis might be recommended in some high risk areas to reduce the risk of getting malaria
- Without chemoprophylaxis, the risk of malaria in travelers is as high as more than 20 % per month in Oceania, and 2 % per month in sub-Saharan Africa ¹

Background

- Although many studies showed high efficacy of chemoprophylaxis, drug compliance is an important factor for effectiveness in the real use
- The number of Thai travelers to Africa has increased in recent years
- The use of malaria prophylaxis in Thai travelers has never been studied before

Objective

Primary objective

1. To determine the **compliance** of malaria chemoprophylaxis among Thai and foreign short-term travelers
2. To find an **incidence of self-reported adverse effects** of mefloquine, doxycycline and atovaquone-proguanil used as malaria chemoprophylaxis among Thai and foreign travelers

Objective

Secondary objective

1. To determine the **factors associated with compliance** of malaria chemoprophylaxis among Thai and foreign travelers
2. To compare the compliance between Thai and foreign travelers

Materials and methods

Study design

- Prospective, cohort study by using questionnaire and telephone interview

Study Site

- Travel Clinic, Hospital For Tropical Diseases, Faculty of Tropical Medicine, Mahidol University

Materials and methods

Study period

- One year after getting approval from the Ethic Committee (2016-2017)

Materials and methods

Inclusion criteria

1. Age between **18 and 70 years**
2. Plan to travel in malaria endemic area **less than 3 months**
3. Plan to take malaria chemoprophylaxis

Materials and methods

Exclusion criteria

1. Pregnancy
2. Contraindication for their use :
 - **Mefloquine** : Hypersensitivity to the drug, active or previous psychiatric disorders, history of seizures
 - **Atovaquone-proquanil** : Hypersensitivity to the drug, breastfeeding woman, severe renal impairment ($\text{CrCl} < 30 \text{ml/min}$)
 - **Doxycycline** : Hypersensitivity to the drug

Materials and methods

Operational definition

- Full compliance : missing $< 10\%$ of all tablets
- Noncompliance : missing $\geq 10\%$ of all tablets

All Thai and foreign travelers who are recommended to take the drug and eligible will be invited to participate in the study



Participants will answer questionnaire by themselves at the first visit



Participants will be followed up by either telephone or e-mail within 1 week after their anticipated date of last tablet

Materials and methods

Sample size calculation

- The calculated sample size is **246 people with 95% CI**

Result

227 travelers were enrolled

4 excluded

147 have been followed

76 waiting for F/U

8 lost F/U

130 completely F/U

9 canceled trip

Analyzed

Table 1 : Demographic characteristics of the participants

Characteristic	Total N=130	Thai N=103	Foreigner N=27
Sex			
Male	67(51.5%)	50(48.5%)	17(63%)
Female	63(48.5%)	53(51.5%)	10(37%)
Age			
<30	26(20%)	20(19.4%)	6(22.2%)
30-45	51(39.2%)	40(38.8%)	11(40.7%)
46-60	39(30%)	34(33.0%)	5(18.5%)
>60	14(10.8%)	9(8.7%)	5(18.5%)
Mean age(years)	42.38	42.41	42.25
Median duration(days)	10	10	15

Table 1 : Demographic characteristics of the participants

Characteristic	Total N=130	Thai N=103	Foreigner N=27
Drug			
Atovaquone /Proguanil	84(64.6%)	66(64.1%)	18(66.6%)
Doxycycline	29(22.3%)	24(23.3%)	5(18.5%)
Mefloquine	17(13.1%)	13(15.6%)	4(14.9%)
Destination			
Africa	108(83.1%)	87(84.5%)	21(77.8%)
Asia	3(2.3%)	2(1.9%)	1(3.7%)
Oceania	15(3.1%)	14(13.6%)	1(3.7%)
South America	4(11.5%)	0	4(14.8%)

Table 1 : Demographic characteristics of the participants

Characteristic	Total N=130	Thai N=103	Foreigner N=27
Purpose			
Leisure			
Backpack	57(42.5%)	40(37.6%)	17(60.9%)
Group tour	28(21.5%)	25(24.3%)	3(11.7%)
Work			
Business	10(7.7%)	9(8.7%)	1(3.7%)
Worker	30(22.6%)	26(24.6%)	4(14.8)
VFR	3(2.3%)	3(2.3%)	0
Volunteer	5(3.4%)	2(7.8%)	3(8.9%)

Table 1 : Demographic characteristics of the participants

Characteristic	Total N=130	Thai N=103	Foreigner N=27
Accommodation			
Luxury hotel	77(44%)	67(48.3%)	10(23.2%)
Budget hotel	19(11%)	10(7.2%)	9(21%)
Guest house	21(12%)	13(9.3%)	8(18.6%)
Local home	17(10%)	11(7.9%)	6(14%)
Camp	40(23%)	38(27.3%)	10(23.2%)
Previous malaria prophylaxis			
No	98(75.4%)	86(83.5%)	12(44.4%)
Yes	32(24.6%)	17(16.5%)	15(55.6%)

Table 1 : Demographic characteristics of the participants

Characteristic	Total N=130	Thai N=103	Foreigner N=27
Previous malaria infection			
No	119(91.5%)	94(83%)	25(92.6%)
Yes	11(8.5%)	9(7%)	2(7.4%)
Current Medication			
No	106(81.5%)	87(84.5%)	19(70.4%)
Yes	24(18.5%)	16(15.5%)	8(29.6%)

Drug compliance

Figure1 : Drug compliance of all participants

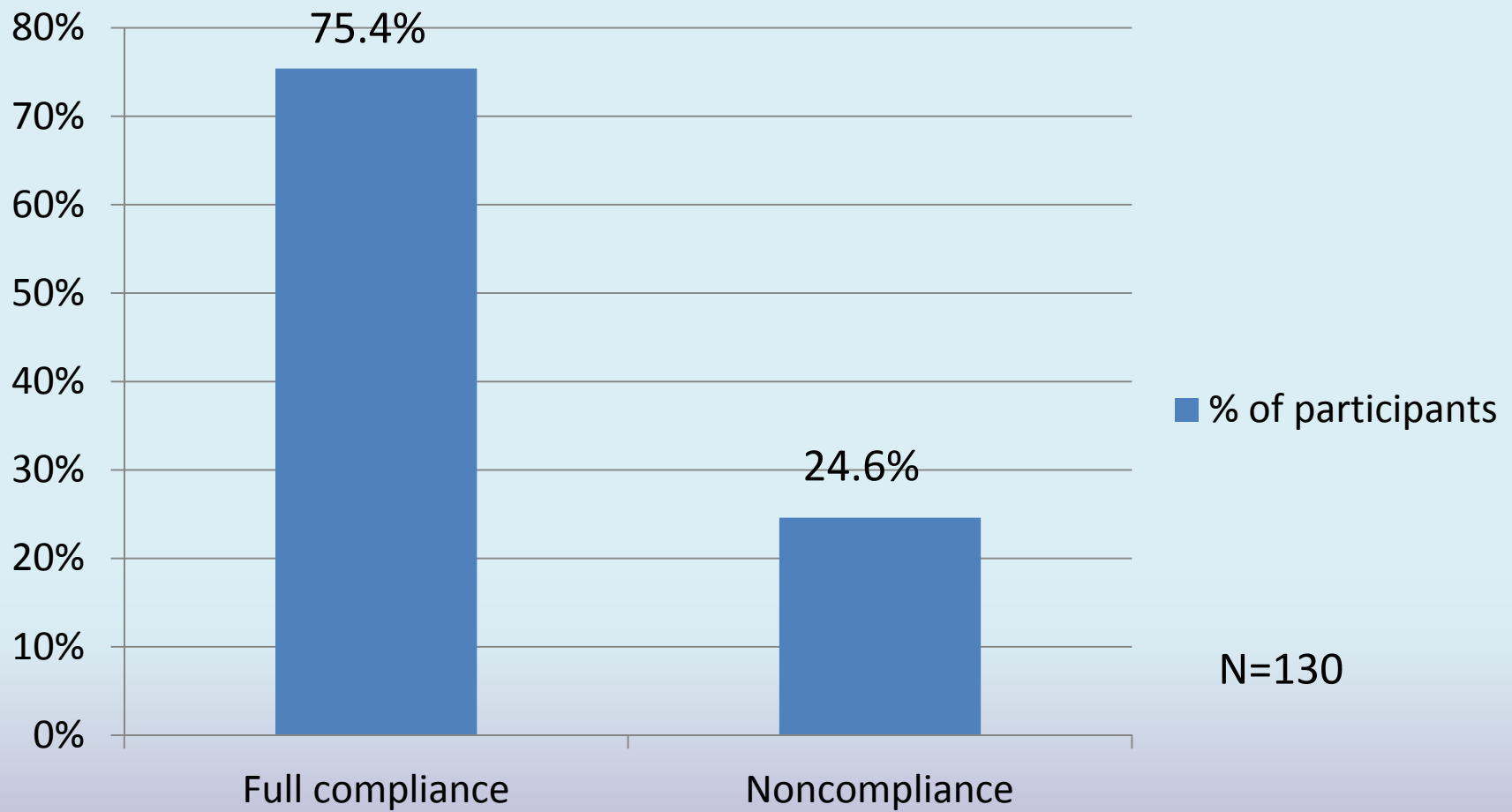


Figure2: Comparison between Thai and Foreign travelers according to compliance

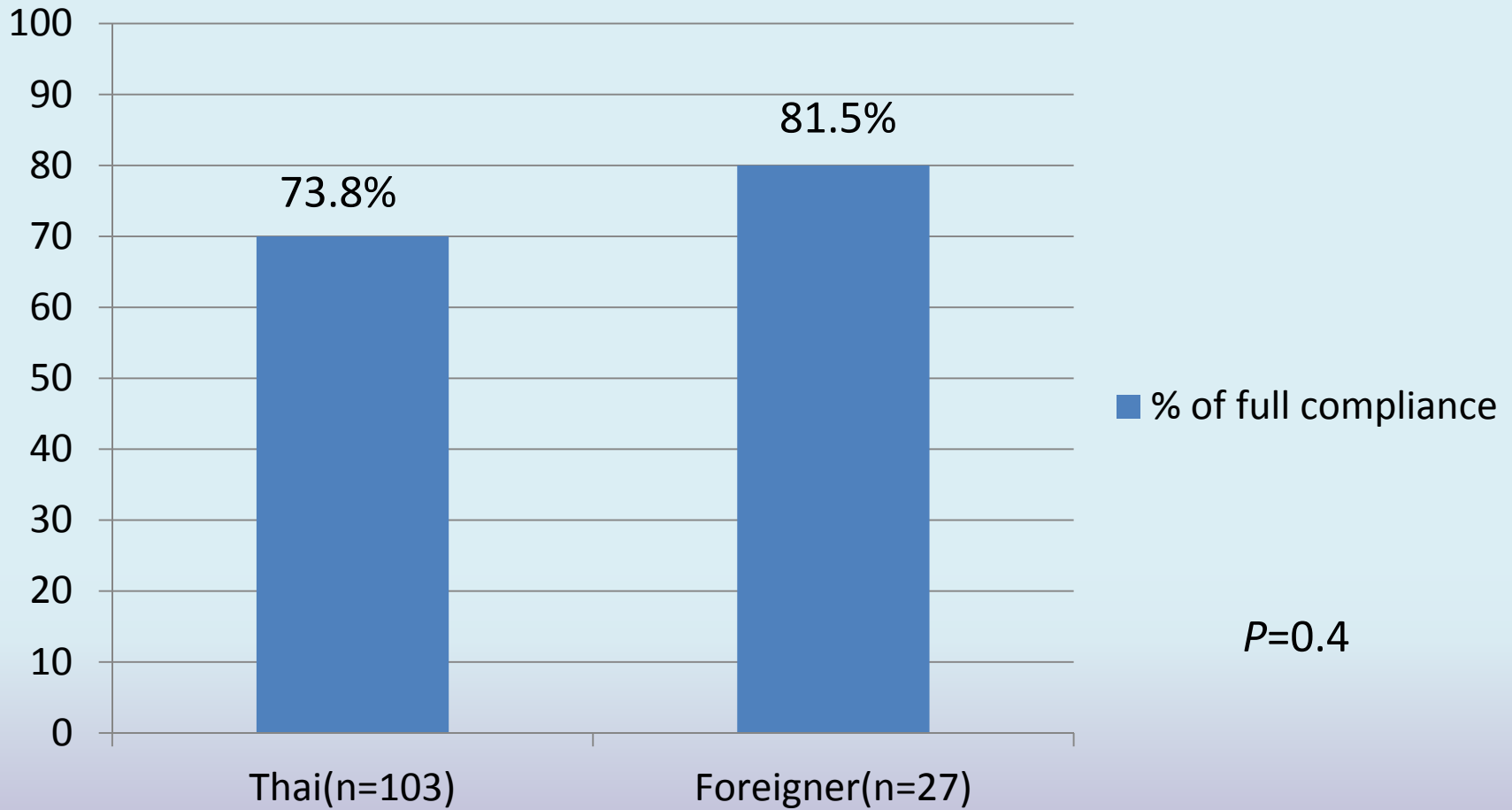


Figure3: Reasons for noncompliance

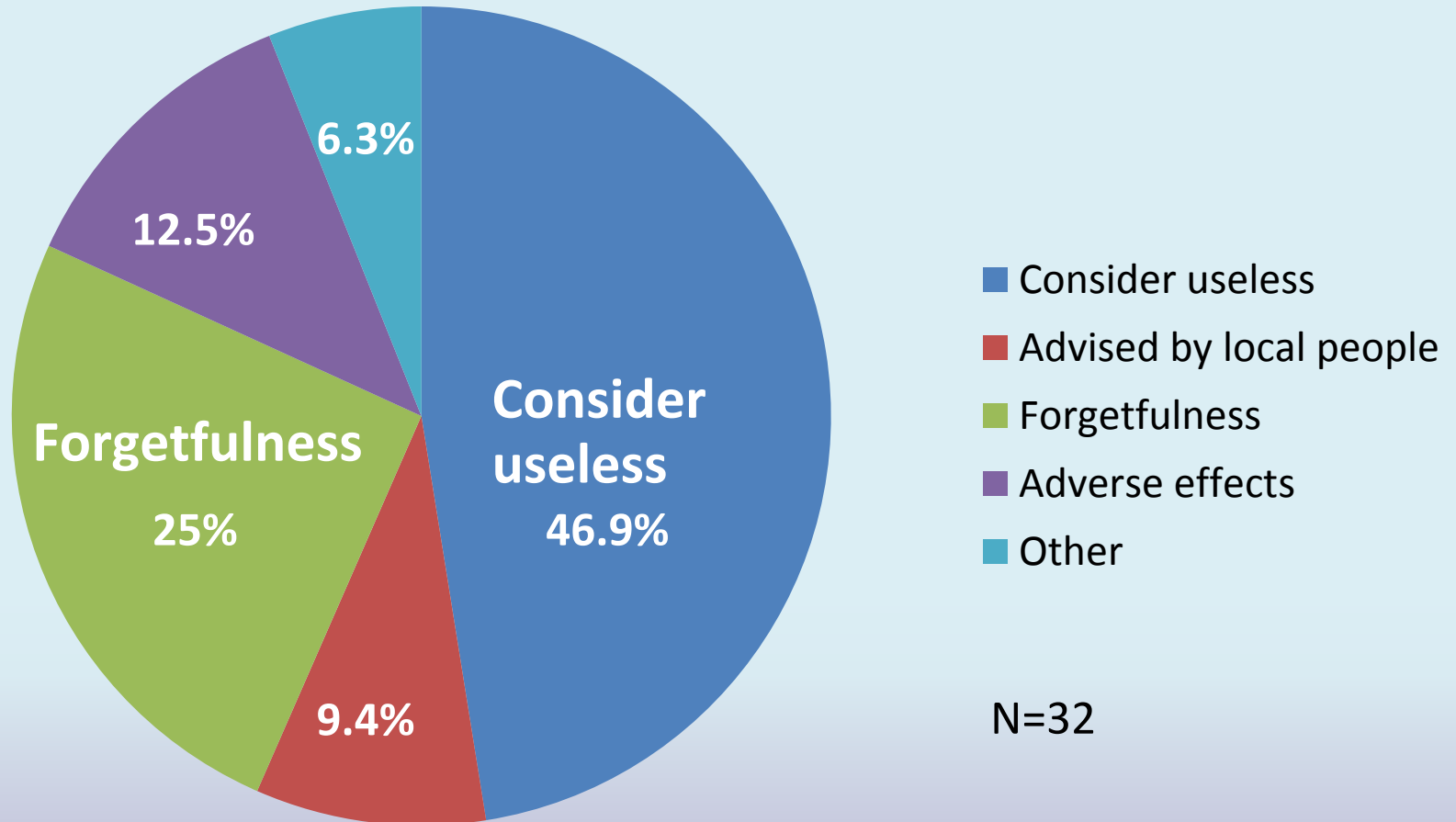


Table 2: Comparison between drugs according to compliance

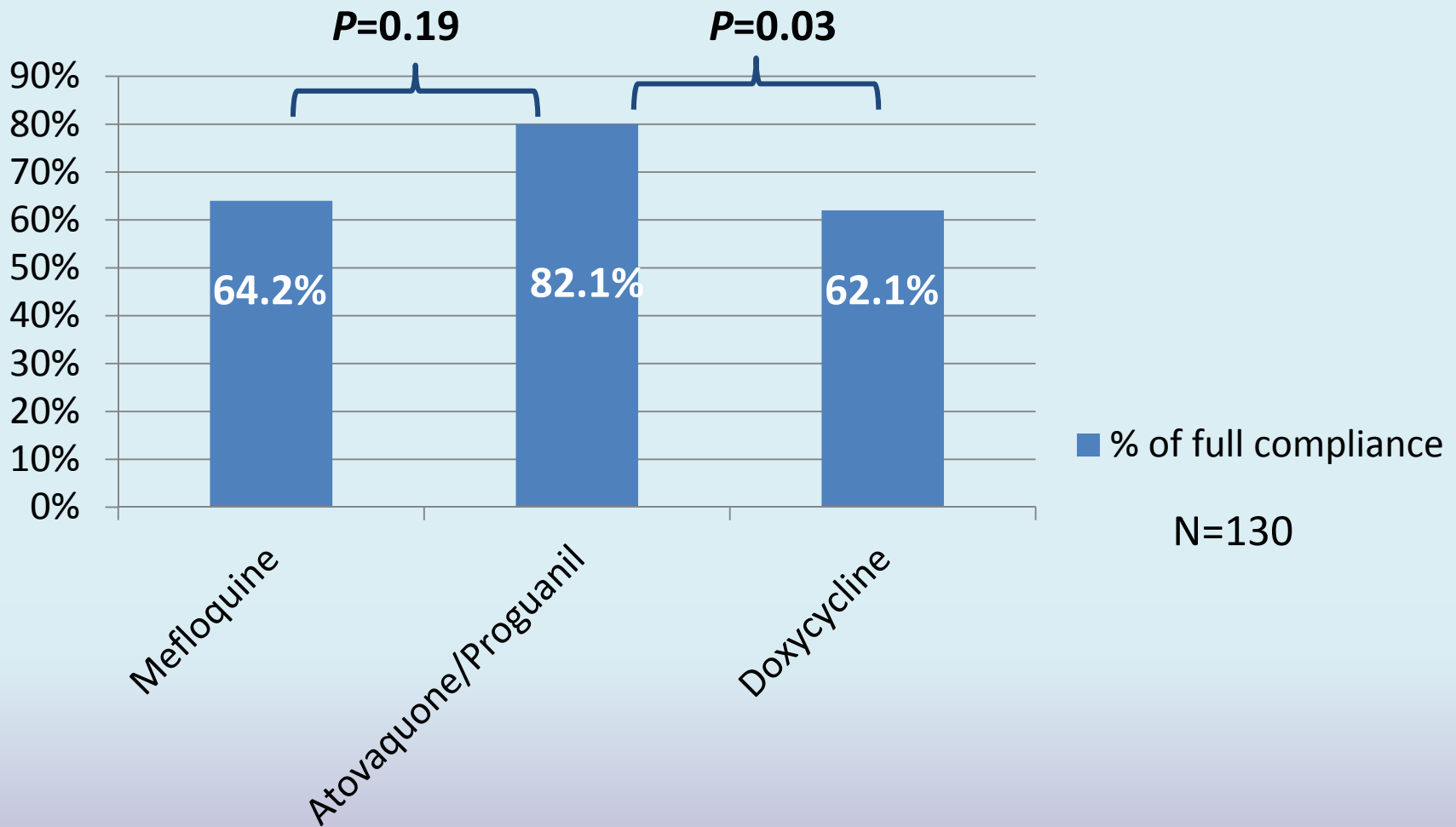


Table2: Comparison between drugs according to compliance

Drug	Compliant	Non compliant	OR	<i>P</i> value
Atovaquone /Proguanil (n=84)	69(82.1%)	15(17.9%)	2.7 (1.19-6.11)	0.016
Doxycycline /Mefloquine (n=46)	29(63%)	17(37%)	1	

Adverse effects

Figure4: Incidence of adverse effects classified by nationality (n=124)

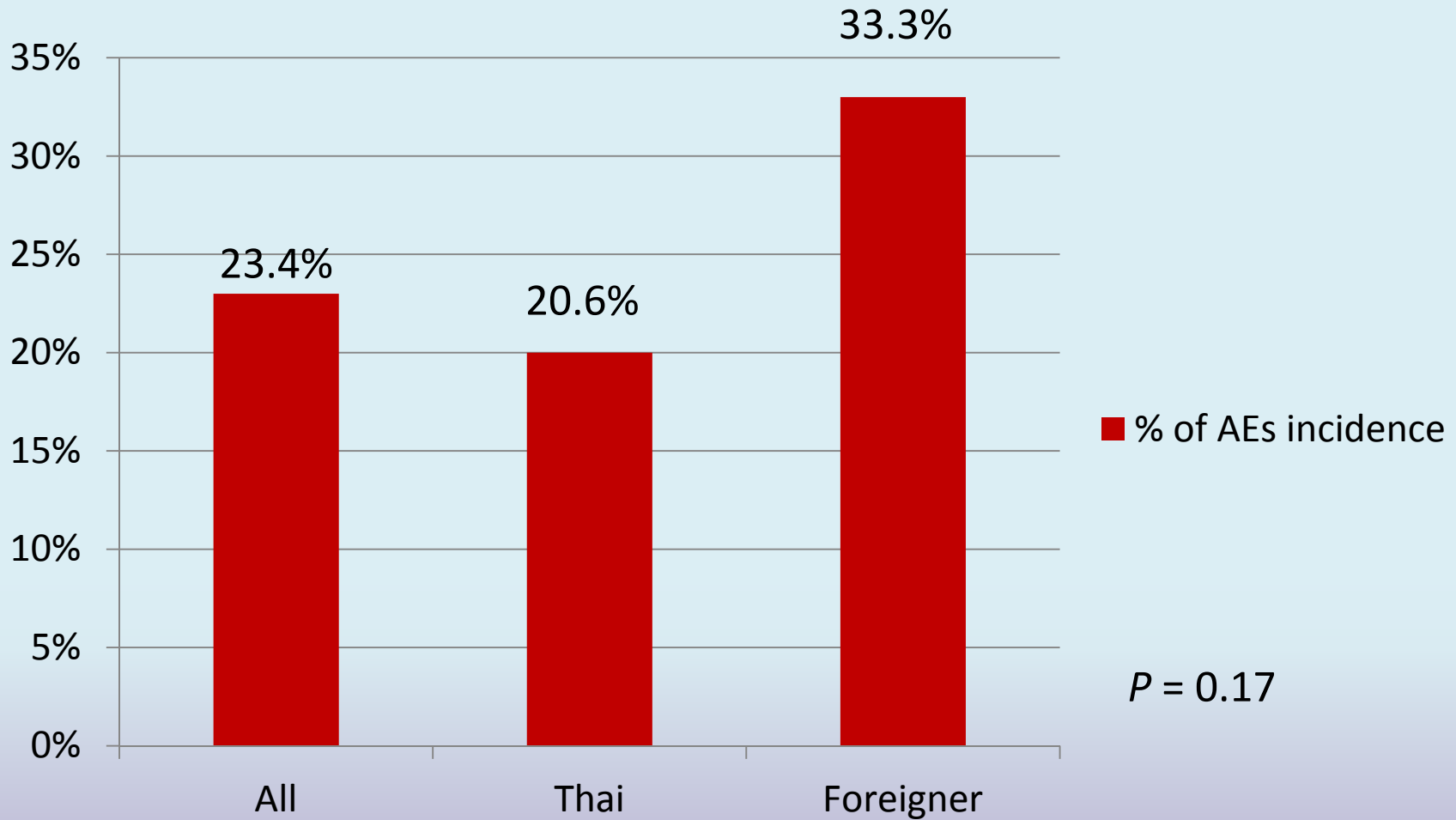


Figure 5 : Incidence of adverse effects classified by drug (n=124)

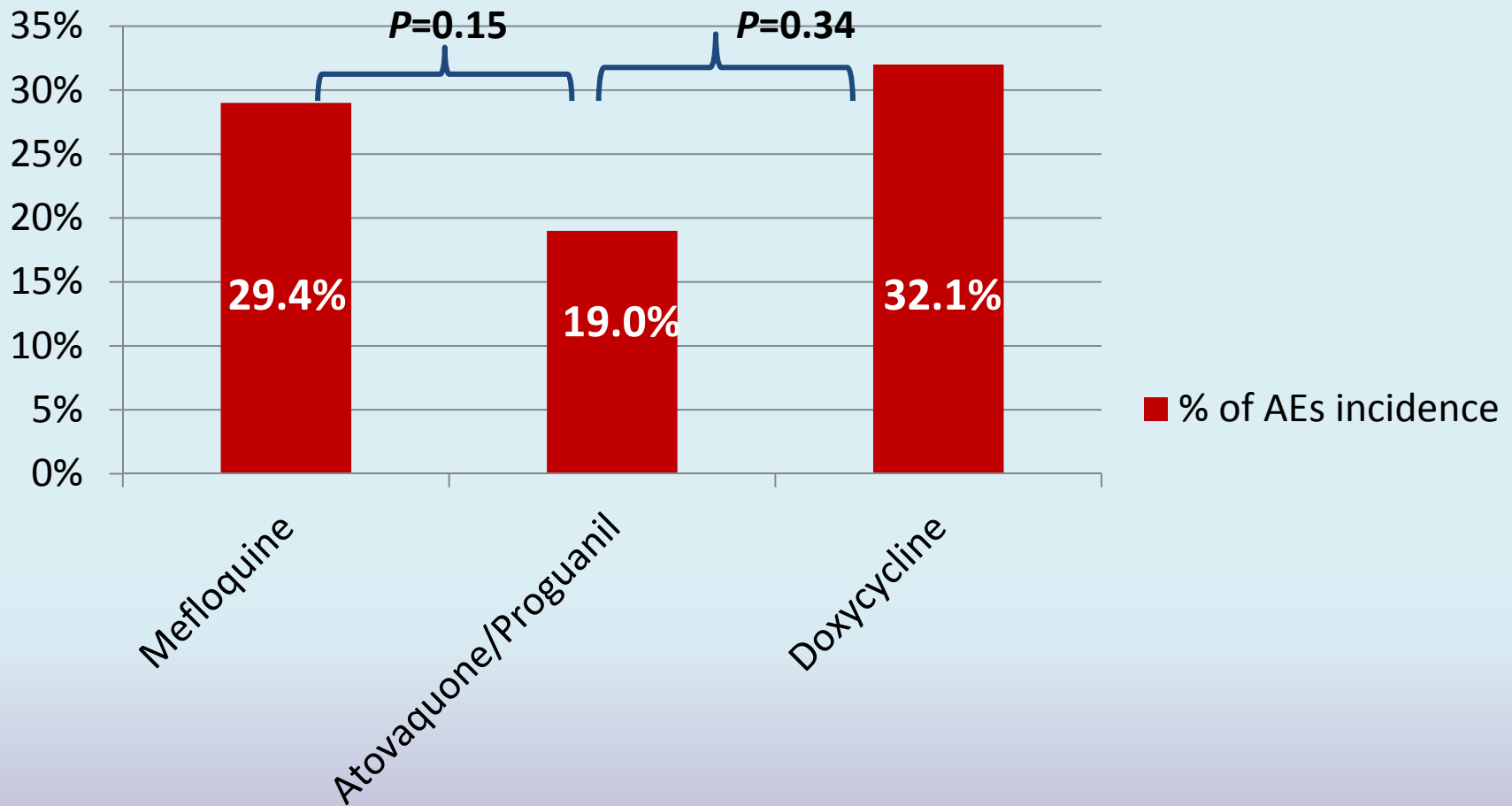


Table 3: Adverse effects from malaria chemoprophylaxis reported by 124 travelers taking different drugs

AEs	Total	Atovaquone /Proquanil	Doxycycline	Mefloquine
	(N=124)	(N=79)	(N=28)	(N=17)
Insomnia	6(4.6%)	1(1.3%)	2(7.1%)	3(17.6%)
Nightmare	5(3.8%)	2(2.5%)	1(3.5%)	2(11.8%)
Headache	4(3.1%)	2(2.5%)	1(3.5%)	1(5.9%)
Dizziness	4(3.1%)	3(3.8%)	1(3.5%)	0
Depression	1(0.8%)	0	1(3.5%)	0
Anorexia	3(2.3%)	3(3.8%)	0	0

Table 3: Adverse effects from malaria chemoprophylaxis reported by 124 travelers taking different drugs

AEs	Total (N=124)	Atovaquone /Proguanil (N=79)	Doxycycline (N=28)	Mefloquine (N=17)
Nausea	8(6.2%)	4(5.1%)	3(10.7%)	1(5.9%)
Vomiting	1(0.8%)	1(1.3%)	0	0
Abdominal pain	5(3.9%)	3(3.8%)	2(7.1%)	0
Diarrhea	4(3%)	2(2.5%)	1(3.5%)	1(5.9%)
Oral ulcer	3(2.3%)	2(2.5%)	0	1(5.9%)
Rash	6(4.6%)	4(5.1%)	2(7.1%)	0
Photosensitivity	1(2.8%)	0	1(3.5%)	0
Vaginal discharge	0	0	0	0
Other	1(0.8%)	1(1.3%)	0	0

Table4: Group of adverse effects from 3 malaria chemoprophylactic drugs

AEs	Total (N=124)	Atovaquone /Proguanil (N=79)	Doxycycline (N=28)	Mefloquine (N=17)
GI	21(16.9%)	13(16.4%)	6(21.4%)	2(11.8%)
Neurological	16(12.9%)	6(7.6%)	5(17.9%)	5(29.4%)
Skin	7(5.6%)	4(5.1%)	3(10.7%)	0

**Factor associated with
drug compliance**

Table 5 : Factors associated with compliance (N=130)

Factors	Compliant	Noncompliant	OR	<i>P</i> value
Sex				
Male	68.7%	31.3%		
Female	82.5%	17.5%	2.16(1.06-4.95)	0.07
Mean age(years)	42.95	40.66		0.38
Travel purpose				
Leisure (Backpack+ Group tour)	80.5%	19.5%	3.85(1.55-9.57)	0.006
Business	90.0%	10.0%	8.4(0.94-75.1)	0.06
Work	48.3%	51.7%		

Table 5 : Factors associated with compliance (N=130)

Factors	Compliant	Noncompliant	OR	<i>P</i> value
Mean duration of travel(days)	15.78	17.38		0.64
Drug				
Atovaquone /Proguanil	82.1%	17.9%	2.7(1.19-6.11)	0.01
Doxycycline / Mefloquine	63.0%	37.0%		
Previous prophylaxis				
No	76.5%	23.5%	1.28(0.52-3.14)	0.6
Yes	71.9%	28.1%		

Table 5 : Factors associated with compliance (N=130)

Factors	Compliant	Noncompliant	OR	P value
History of malaria				
No	73.1%	26.9%		
Yes	100%	0	RR=0.73(0.66-0.82)	0.07
Mosquito protection				
No	85.7%	14.3%	2.1(0.44-9.9)	0.52
Yes	74.1%	25.9%		
Current Medication				
No	76.4%	23.6%	1.33(0.5-3.58)	0.57
Yes	70.8%	29.2%		

Conclusion for preliminary result

- 75% of participants had good compliance to chemoprophylaxis
- Compliance in Thai and foreign travelers were not different (73.8% vs. 81.5%, $P=0.4$)
- 23% of travelers displayed adverse effects
- The most common adverse effect was GI symptoms (16.9%)

Conclusion for preliminary result

- Travel purpose and type of chemoprophylactic drug might be the associated factors with the compliance

Thank you

