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ANTIMALARIAL USE AND THE ASSOCIATED FACTORS IN RURAL NIGERIA FOLLOWING IMPLEMENTATION OF AFFORDABLE MEDICINES FACILITY-MALARIA (AMFM) PRICE SUBSIDY

RUNNING TITLE: ANTIMALARIAL USAGE FOLLOWING AMFM SUBSIDY

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ABSTRACT

Purpose

This study was set out to find out the pattern of antimalarial drug use in a Nigerian rural community following the aggressive price subsidy of Artemisinin Combination Therapy (ACT) recently embarked upon by Roll Back Malaria partners through Affordable Medicines Facility-malaria (AMFm).

Methods

Questionnaires were administered to 310 adult members of the community with the most recent malaria episodes so as to find out about the drugs used and some of the factors associated with the choice of the drug.

Result

Although the overall use of ACT (13.55%) in this community was about 4 times higher than what it used to be, Chloroquine 123 (39.62%) and sulphadoxine/pyrimethamine 120 (38.71%) were the mostly used antimalarial agents. Choice of drug used was significantly associated with perception of efficacy and price among other factors. Respondents liked the price of ACT (33.3%) most, CQ was the drug most liked in terms of efficacy (44.2%) while SP was the drug most liked in terms of lack of side effect (38.9%), taste (61.6%) and convenience (35.7%). (P = 0.001)

Conclusion

In addition to sustaining the current price control, there is a need to continuously monitor and effectively regulate the quality of the ACTs in circulation so as to gain the confidence of both the prescribers and the end users regarding efficacy and adherence to ACTs. This will help to safeguard the huge investment in ACT subsidy by the Roll Back Malaria partners.

Key words: ACT, Subsidy, Affordable Medicines Facility-malaria

INTRODUCTION

The 2008 World Malaria Report showed that only 3% of children with suspected malaria were treated with Artemisinin Combination Therapy (ACT), suggesting that many children were still receiving chloroquine and sulphadoxine/pyrimethamine for malaria treatment despite the recommended change in treatment guidelines [1]. A published study that evaluated 21 African countries for their antimalarial use in 2006-2007 showed that only three countries reported high use of the regimen that was in agreement with the national treatment guideline [2]. The study further revealed that chloroquine was the most common anti-malarial reported in 14 of 21 countries, and reported use was particularly high in West Africa.

A descriptive study that evaluated the anti-malarial drug prescribing practice in private and public health

facilities in South-East Nigeria also showed that only 3.0% of patients were treated with artemisinin combination therapy. Most of the patients were treated with chloroquine (30.2%), sulphadoxine/pyrimethamine (22.7%) or artemisinin monotherapy (15.8%) despite the change in the national malaria treatment policy [3].

Treatment of malaria in pregnancy was not exempted from the protocol violation. A recent survey of the patterns of anti-malarial drug treatment among pregnant women in Uganda showed that only 5.6% of the pregnant women in their first semester were treated according to the national guideline while 70% were treated with contraindicated anti-malarial drugs. Recommended antimalarial were used according to the guidelines in only 30.1% of all second and third trimester episodes [4]. Some of the factors that that

have been found to positively influence the use of clinical guidelines include clarity of guidelines, strong evidence, adequate funding of guidelines and support by opinion leaders especially professional bodies [5]. The reluctance to abandon chloroquine is based, in part, on its low cost, wide availability, and acceptance. Chloroquine results in rapid initial improvement of clinical symptoms, which has contributed to its widespread acceptance and the perception that it remains effective, leading to an unwillingness of both health workers and patients to discontinue using chloroquine despite its reduced efficacy [6]. In 2004, Nigeria changed from the use of chloroquine and sulphadoxine/pyrimethamine as first line anti-malarial drugs in line with the recommendation of the World Health Organization as a result of unacceptably high level of resistance to the formal drugs [7]. Adherence of patients as well as health care providers to the new guidelines remain poor in many parts of Nigeria [8-10].

Research data from Kenya provided strong evidence that continued use of chloroquine in areas with resistance was contributing to excess *Plasmodium falciparum* related deaths [6]. Apart from vector and parasite biology, pharmacokinetics, and economics reasons; human behavior is another factor that has been associated with antimalarial drug resistance [11]. In addition to low usage of ACTs imposed by its high cost, quality of ACTs in circulation is another major challenge. Recent survey by the World Health Organization (WHO) in conjunction with Nigerian drug regulation agency showed that Nigeria has the highest rate of sub-standard antimalarials (63.9%) in Sub-Saharan Africa [1]. The survey further revealed that a common problem for ACTs was that of lower content of active pharmaceutical ingredients (APIs). This was further supported by the findings of the Global Funds which showed that availability of quality-assured ACTs in Nigeria is only 28% [1].

The first attempt to improve the use of ACT in Nigeria was in 2008 when the government took a step forward in subsidizing child doses of Amodiaquine-artesunate combination (ASAQ) via the private sector in 18 of the 37 states. Retailers in these 18 states could purchase subsidized ACTs for 5 naira (\$0.03 USD) per treatment with an approved retail price set at 30 naira (\$0.20 USD). This was followed by widespread stockouts of ACTs across Nigeria as a result of inadequate supply. This resulted in reduced availability of ACTs in the public sector and increased prices in the private sector. End users were eventually forced to revert back to the cheaper monotherapy [13].

Efforts to remove the obstacle imposed by high cost and stockouts of ACTs received another boost when Nigeria initiated Affordable Medicines Facility-malaria (AMFm) activities on October 5, 2010. AMFm was set by the Roll Back Malaria Partnership (RBM) in 2007 and managed by the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund).

The AMFm aims to increase use of ACTs by subsidizing prices of ACTs at the "factory gate". The subsidy will in turn be passed along the supply chain to the consumer, lowering ACT prices so that they are comparable to chloroquine, sulfadoxine-pyrimethamine or artemisinin monotherapy. Reduced prices should, in theory, "crowd out" sales of these other drugs and thus increase ACT use [13].

The aim of this study is to find out the current malaria treatment practices following the introduction of AMFm and some of the factors that are associated with such practices in a rural community in South-West Nigeria.

METHODS

This study was carried out between March and April 2012 at Oke-icho, a rural community in Oyo State, South-West Nigeria with a population of about 12,964 inhabitants. It is situated at 8.03° North latitude, 3.35° East longitude and 314 meters elevation above the sea level, the climate is tropical rainforest with malaria transmission occurring most of the year [13-14]. Information about the number of streets and houses in this community was obtained from the local government authority. Eleven houses were randomly selected from each street by simple random sampling method, and then an adult with the most recent episode of malaria was chosen as participant per house after informed consent was obtained. Pretested questionnaires were administered by trained research assistants to participants after translation of the contents to their local dialects.

Statistical analysis

Data was analyzed with the free GNU PSPP Statistical Analysis Software version 0.7.9-gd4ae90. Using the descriptive statistics in the analysis command, frequency tables were generated for the general characteristics of the participants and expressed in percentages. Association between the drug used to treat the last malaria episode and other variables was assessed using Chi-Square, and $p < 0.05$ was taken to be significant.

RESULTS

Majority (58.71%) were females while 201 (64.84%) were married (table 1). Malaria was the 4th common health problem 49 (15.16%) experienced by participants and it was experienced once to twice a

year in most cases (41.61%) presenting as fever 126 (40.65%) and headache 86 (27.74%)(Table 2).

TABLE 1: SOCIODEMOGRAPHIC PARAMETER OF THE RESPONDENTS

Character	frequency	%
Age		
18-20	50	(16.13)
21-30	114	(36.77)
31-40	87	(28.06)
41-50	31	(10.02)
>50	28	(9.03)
Sex		
Male	128	(41.24)
Female	182	(58.71)
Marital status		
Married	201	(64.84)
Single	09	(35.16)
Separated	0	(0)
Level of education		
No formal education (Nil)	27	(8.71)
Primary school certificate	40	(12.90)
Secondary school certificate	163	(52.58)
Diploma	69	(22.26)
Degree	11	(3.55)
Occupation		
Unemployed	0	(3.23)
Students	68	(21.94)
Trading	81	(26.13)
Farming	20	(6.45)
Artisan	61	(19.68)
Teaching	37	(11.94)
Apprentice	7	(2.26)
Civil servants	10	(3.23)
Others	16	(5.16)
Tribe		
Yoruba	284	(91.61)
Ibo	7	(2.26)
Hausa	14	(4.52)
Fulani	4	(1.27)
Ghanaian	1	(0.32)

Sulphadoxine/pyrimethamine 92(29.68%) was mostly regarded as the currently recommended drug for treating malaria followed by chloroquine 85(27.42%). The drug used to treat the last episode of malaria by respondents included chloroquine 123(39.62%), sulphadoxine/pyrimethamine 120(38.71%), ACT 82(13.55%) and Artesunate monotherapy 8 (2.58%) (Table 3). CQ was mostly used by males (42.2%) while SP was mostly used by females (39.0%).

Use of ACT observed among females (15.9%) was about 1.6 times higher than in the males (10.2%), $p=0.56$. While the use of SP has no definite pattern with

the level of education, ACT use increased with the level of education, with the highest among those with university degree (27.2%) while the use of CQ was highest among those with no formal education 14 (15.8%), $P=0.33$, (Table 4).

TABLE 2: MALARIA FEATURES AMONG PARTICIPANTS

Features	Frequency	%
What is your commonest health problem?		
Headache	95	(30.65)
Back pain	50	(16.13)
General body aches	94	(30.32)
Malaria	49	(15.16)
Menstrual pain	3	(0.79)
Abdominal pain	2	(0.65)
Others	19	(6.13)
How often do you experience malaria attack?		
< once per year	39	(12.58)
1-2 times per year	29	(41.61)
3-4 times per year	91	(29.35)
4-6 times per year	49	(15.81)
>6 times per year	2	(0.65)
What major sign suggest that you have malaria?		
Fever	126	(40.65)
Headache	86	(27.74)
Diarrhea	11	(3.55)
Loss of appetite	50	(16.13)
Body weakness	36	(11.61)
Others	1	(0.32)

Friends 7(50.0%) and Chemists 15 (33.3%) were more likely to prescribe CQ than any other drug. Doctors 26 (19.3%) were the most likely to prescribe ACT followed by nurses (15.4%). $P=0.001$. ACT was mostly liked for its good price (33.3%), CQ was the drug mostly liked in terms of efficacy (38.1%) while SP was the drug mostly liked in terms of lack of side effect (38.9%), taste (61.6%) and convenience (35.7%). $P=0.001$.

The use of CQ 76(89.4%) and SP 70(76.1%) were highest among those who believed that they were the recommended drugs for malaria while ACT 10(55.5%) use was also highest among those who were of the opinion that it was the current antimalarial of choice. $P=0.001$. (Table 5).

DISCUSSION

The overall use of ACT(13.55%) in this community was about 4 times higher than recorded in 2008 [1]. This may be a reflection of user's satisfaction with the

price and probably improved availability following implementation of AMFm .

The higher rate of ACT use and the lower rate of CQ use among females compared to males in this study may be due to the fact that females are more likely to receive health education regarding malaria control as a result of antenatal care visit [15-16].

TABLE 3: KNOWLEDGE AND ATTITUDE TOWARD MALARIA TREATMENT.

Knowledge/Attitude	frequency	%
What is the currently recommended drug in malaria treatment policy?		
Chloroquine	85	(27.42)
S/P-Fansidar, Amalare.t.c	92	(29.68)
ACT e.gCoartem	18	(5.81)
Artesunate alone	18	(5.81)
Ampicilin	32	(10.32)
Cotrimoxazole	28	(9.03)
Others	37	(11.94)
Drug used during the last episode of malaria?		
Chloroquine	123	(39.62)
S/P-Fansidar, Amalare.t.c	120	(38.71)
ACT e.gCoartem	42	(13.55)
Artesunate alone	8	(2.58)
Ampicilin	7	(2.26)
Cotrimoxazole	5	(1.61)
Others	5	(1.61)
Who prescribe the drug to you?		
Doctor	133	(42.90)
Nurse	39	(12.62)
Chemist	73	(23.62)
Self	48	(15.53)
Friend	16	(5.16)
What did you like most about the used drug?		
Good price	15	(4.84)
Efficacy	231	(74.52)
No side effect	18	(5.81)
Taste	18	(5.81)
Convenient.	28	(9.02)

S/P= Sulphadoxin-Pyrimethamine,
ACT=ArtemisininCombination Therapy.

Though closely followed by SP 4(26.7%) and CQ 3(20.0%), the fact that the price of ACT 5(33.3%) was what users liked most about these drugs suggested that effect of the recent aggressive subsidy mechanism by AMFm to lower the price ACT is being felt in this part of the country [13].

Surprisingly, participants rated the efficacy of CQ (44.2%) and SP (38.1%) above that of ACT (12.6%) contrary to available evidence from clinical trials [17-18]. This may explain why these older drugs were still

largely used in this community despite the perceived satisfaction with the price of ACT.

This contradiction is probably because therapeutic efficacy trials evaluate clinical and laboratory evidence in children below the age of 5 years while this study sought testimonies of adult antimalarial users. It may also be due to the fact that ACTs used in therapeutic efficacy trials are usually of certified quality [19] while drugs used by patients come from the open market. The latter possibility is supported by the recent findings of widespread substandard and fake ACTs in Nigerian drug market [12-13]. Testimonies of the end users may also explain the observed high rate of CQ and SP prescription by doctors and nurses in this study.

Conclusion

This study showed that though chloroquine and sulphadoxine/pyrimethamine were still the major anti-malarial drugs currently used in this part of Nigeria, there was an improvement in ACT use when compared to years before AMFm implementation. Antimalarial use practices are significantly associated with who prescribe the drugs, knowledge of the current treatment guidelines as well of perception of efficacy by the users. Users liked the price of ACT but still believed in the efficacy of the older drugs. In addition to sustaining the current price control, there is a need to continuously monitor and effectively regulate the quality of the ACTs in circulation so as to gain the confidence of both the prescribers and the end users regarding efficacy and adherence to ACTs. This will help to safeguard the huge investment in ACT subsidy by the Roll Back Malaria partners.

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Conflict of Interest

We declare that there are no conflicts of interest associated with this study

Contribution of Authors

We declare that this work was done by all the 6 authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Authors AME and AF conceived the study. Authors EAM, FA, KB andMOB designed the study. The data presented in this study was collected and analyzed by Authors; EAM, OOO, MOB andOEI. The write-up was done by EAM and KB.

TABLE 4-: RELATIONSHIP BETWEEN SOCIODEMOGRAPHIC PARAMETERS OF THE PARTICIPANTS AND THE DRUG USED TO TREAT THE LAST MALARIA EPISODE.

(Drug used during the last episode of malaria)									
CQ	S/P	ACT	AM	Amp	Cotrim	Others	Total (%)	Frequency (%)	
Age									
18-20		22(44.0)	19(38.0)	1(2.0)	2(4.0)	2(4.0)	2(4.0)	2(4.0)	50(100)
21-30		42(36.8)	47(41.2)	15(13.2)	5(4.4)	4(3.5)	0(0.0)	1(0.9)	114(100)
31-40		29(33.3)	34(39.1)	19(21.8)	1(1.1)	1(1.1)	2(2.3)	1(1.1)	87(100)
41-50		14(45.2)	12(38.7)	5(16.1)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	31(100)
>50		16(57.1)	8(28.6)	2(7.1)	0(0.0)	0(0.0)	1(3.6)	1(3.6)	28(100)
Pearson Chi Square = 33.65, <i>df</i> = 36, <i>P</i> = 0.58									
Sex									
Male		54(42.2)	49(38.1)	13(10.2)	5(3.9)	2(1.6)	3(2.3)	2(1.6)	128(100)
Female		69(37.9)	71(39.0)	29(15.9)	3(1.6)	5(2.7)	2(1.1)	3(1.6)	182(100)
Pearson Chi Square = 4.89, <i>df</i> = 6, <i>P</i> = 0.56									
Level of education									
Nil		14(51.8)	10(37.0)	1(3.7)	0(0)	0(0)	1(3.7)	1(3.7)	27(100)
Primary	21(52.5)	12(30.0)	3(7.5)	2(5.0)	1(2.5)	1(2.5)	0(0)	40(100)	Secondary 63(38.7)
68(41.7)	19(11.7)	3(1.8)	6(3.7)	1(0.6)	3(1.8)	163(100)			
Diploma		21(30.4)	26(37.7)	16(23.2)	3(4.3)	0(0)	2(2.9)	1(1.4)	69(100)
Degree		4(36.4)	4(36.4)	3(27.2)	0(0)	0(0)	0(0)	0(0)	11(100)
Pearson Chi Square = 26.54, <i>df</i> = 24, <i>P</i> = 0.33									

CQ-chooroquine, S/P -sulphadoxin/pyrimethamine, ACT -Artemisinin combination therapy, AM- Artesunate monotherapy, Amp - Amoxicillin, Cotrim-Cotrimoxazole.

TABLE 5: RELATIONSHIP BETWEEN THE DRUGS USED TO TREAT THE LAST MALARIA EPISODE AND THE DRUG PRESCRIBER, WHAT THE USER LIKED MOST ABOUT THE DRUG AND THE USER'S KNOWLEDGE OF CURRENTLY RECOMMENDED ANTI-MALARIA DRUGS.

(Drug used during the last episode of malaria)								
CQ	S/P	ACT	AM	Amp	Cotrim	Others		
Frequency (%)								
Who prescribed the used drug								
Friend		7(5.7)	3(2.5)	1(2.4)	1(12.5)	2(28.6)	1(20.0)	1(20)
Doctor		52(42.3)	56(49.1)	24(57.1)	1(12.5)	0(0)	0(0)	0(0) Nurse
16(13.0)	16(13.4)	6(14.3)	1(12.5)	0(0)	0(0)	0(0)	0(0)	Chemist
32(26.0)	29(24.4)	4(9.7)	4(50.0)	1(14.3)	3(60.0)	0(0)	0(0)	Self
16(13.0)	15(12.6)	7(16.7)	1(12.5)	4(57.1)	1(20.0)	4(80)	Total	
123 (100)	120(100)	42(100)	8(100)	7(100)	5(100)	5(100)	Pearson Chi Square	
52.46, $df = 24, P = 0.001$								
What do you like most about the drug used?								
Cheap price		3(2.4)	4(3.3)	5(11.9)	1(12.5)	0(0)	2(40.0)	0(0)
Efficacy		102(82.9)	88(73.3)	29(69.0)	3(37.5)	3 (42.9)	2(40.0)	4(80.0)
No Side effect		6(4.9)	7(5.8)	4(9.5)	0(0)	0(0)	1(20.0)	0(0)
Taste		3(2.4)	11(9.2)	0(0)	2(25.0)	2(28.6)	0(0)	0(0)
Convenience		9(7.3)	10(8.3)	4(9.5)	2(25.0)	2(28.6)	0(0)	1(20.0)
Total		123 (100)	120(100)	42(100)	8(100)	7(100)	5(100)	5(100)
Pearson Chi Square 52.24, $df = 24, P = 0.001$								
Currently recommended drug in malarial treatment policy,								
Chloroquine		76(61.8)	6(5.0)	3(7.1)	0(0)	0(0)	0(0)	0(0)
S/P		7(5.7)	70(53.8)	10(23.8)	3(37.5)	0(0)	2(40.0)	0(0)
ACT		3(2.4)	4(3.3)	10(23.8)	0(0)	1(14.3)	0(0)	0(0)
AM		2(1.6)	3(2.5)	11(26.2)	0(0)	1(14.3)	0(0)	1(20.0)
Ampicilin		11(8.9)	10(8.3)	2(4.8)	4(50.0)	2(28.6)	1(20.0)	2(40.0)
Cotrimoxazole		7(5.7)	17(14.2)	0(0)	1(12.5)	2(28.6)	0(0)	1(20.0)
Others		17(13.8)	10(8.2)	6(14.3)	0(0)	1(14.3)	2(40.0)	1(20.0)
Total		123 (100)	120(100)	42(100)	8(100)	7(100)	5(100)	5(100)
Pearson Chi Square 258.52, $df = 36, P = 0.001$								

CQ-chloroquine, S/P -sulphadoxin/pyrimethamine, ACT -Artemisinin combination therapy,

AM- Artesunate monotherapy, Amp - Amoxicillin, Cotrim-Cotrimoxazole

REFERENCES

- World Health Organization: World Malaria Report: Interventions to Control Malaria. WHO. 2008.
- Frosch AEP, Venkatesan M, Laufer KM. Patterns of chloroquine use and resistance in sub-Saharan Africa: a systematic review of household survey and molecular data. *Malar J* 2011;10:116-126
- Meremikwu M, Okomo U, Nwachukwu C, Oyo-Ita A, Eke-Njoku J, Okebe J, Oyo-Ita E, Garner P. Antimalarial drug prescribing practice in private and public health facilities in South-east Nigeria: a descriptive study. *Malar J* 2007; 6:55-58
- Sangaré RL, Weiss NS, Brentlinger PE, Richardson BA, Staedke SG, Kiwuwama MS, Stergachis A. Patterns of anti-malarial drug treatment among pregnant women in Uganda. *Malar J* 2011; 10:152-160
- West P, Wright D, Wright J. What's the evidence that NICE guidance has been implemented? Results from a national evaluation using time series analysis, audit of patients' notes, and interviews *BMJ* 2004; 329:999-1007.
- Zucker RJ, Ruebush KT, Obonyo C, Otieno J, and Campbell CC. The mortality consequences of the

- continued use of chloroquine in Africa: Experience in Siaya, Western Kenya. *Am J Trop Med Hyg* 2003; 68: 386-390
7. World Health Organization. World malaria report 2011.
8. Efunshile M, TamramatRunsewe-Abiodun, BeniamGhebremedhin WolfgangKoenigand Brigitte Koenig. Prevalence of the molecular marker of chloroquine resistance (pfcr76) in Nigeria 5 years after withdrawal of the drug as first-line antimalarial: A cross-sectional study *SAJCH* 2011; 5: 39-41
9. Ukwe CV, Ekwunife OI. Drug utilisation study of antimalarials for the treatment of hospitalised children under five in south-eastern Nigeria. *Pharmacoepidemiol Drug Saf* 2008; 17:1183-1188.
10. Etuk EU, Egua MA, Muhammad AA. Prescription pattern of antimalarial drugs in children below 5 years in a tertiary health institution in Nigeria. *Ann Afr Med* 2008; 7: 24-28.
11. Bloland PB. Drug resistance in malaria. World Health Organization. 2001
12. Survey of the quality of selected antimalarial medicines circulating in six countries of sub-Saharan Africa. Quality Assurance and Safety: Medicines Essential Medicines and Pharmaceutical Policies. WHO. 2011.
13. Bate I R, Hess K, Tren R, Mooney L, Cudjoe F, Ayodele T, Attaran A. Subsidizing artemisinin-based combination therapies: a preliminary investigation of the Affordable Medicines Facility - malaria. *Research and Reports in Tropical Medicine* 2012; 3: 1-6.
14. Population and location of Oke-iho. Downloaded of 28-08-2012 from <http://www.maps-streetview.com/Nigeria/Oke-Iho>
15. World Health Organization. A strategic framework for malaria prevention and control during pregnancy in the African region, Brazzaville: WHO Regional Office for Africa. WHO. 2004.
16. Ouma P, Van Eijk AM, Hamel MJ, Parise M, Ayisi JG, Otieno K, Kager PASlutsker L. Malaria and anaemia among pregnant women at first antenatal clinic visit in Kisumu, western Kenya. *Tropical Medicine and International Health* 2007; 12 :1515-1523.
17. Michael OS, Gbotosho GO, Folarin OA, Okuboyejo T, Sowunmi A, Oduola AMJ. HappiCT. Early variations in *Plasmodium falciparum* dynamics in Nigerian children after treatment with two artemisinin-based combinations: implications on delayed parasite clearance. *Malar J* 2010; 9:335-343
18. Gbotosho GO, Sowunmi A, Okuboyejo TM, Happi CT, Folarin OA, Michael OS, Adewoye EO. Therapeutic efficacy and effects of artemether-lumefantrine and artesunate-amodiaquine formulated or copackaged on malaria-associated anemia in children with uncomplicated *Plasmodium falciparum* malaria in Southwest Nigeria. *Am J Trop Med Hyg* 2011; 84:813-819.
19. World Health Organization Methods for surveillance of antimalarial drug efficacy. WHO Geneva. 2009.