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What determines providers' stated preference for the treatment of uncomplicated malaria? $\stackrel{\text{\tiny{\sc def}}}{=}$



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ABSTRACT

As agents for their patients, providers often make treatment decisions on behalf of patients, and their choices can affect health outcomes. However, providers operate within a network of relationships and are agents not only for their patients, but also other health sector actors, such as their employer, the Ministry of Health, and pharmaceutical suppliers. Providers' stated preferences for the treatment of uncomplicated malaria were examined to determine what factors predict their choice of treatment in the absence of information and institutional constraints, such as the stock of medicines or the patient's ability to pay.

518 providers working at non-profit health facilities and for-profit pharmacies and drug stores in Yaoundé and Bamenda in Cameroon and in Enugu State in Nigeria were surveyed between July and December 2009 to elicit the antimalarial they prefer to supply for uncomplicated malaria. Multilevel modelling was used to determine the effect of financial and non-financial incentives on their preference, while controlling for information and institutional constraints, and accounting for the clustering of providers within facilities and geographic areas.

69% of providers stated a preference for artemisinin-combination therapy (ACT), which is the recommended treatment for uncomplicated malaria in Cameroon and Nigeria. A preference for ACT was significantly associated with working at a for-profit facility, reporting that patients prefer ACT, and working at facilities that obtain antimalarials from drug company representatives. Preferences were similar among colleagues within a facility, and among providers working in the same locality. Knowing the government recommends ACT was a significant predictor, though having access to clinical guidelines was not sufficient.

Providers are agents serving multiple principals and their preferences over alternative antimalarials were influenced by patients, drug company representatives, and other providers working at the same facility and in the local area. Efforts to disseminate drug policy should target the full range of actors involved in supplying drugs, including providers, employers, suppliers and local communities.

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Introduction

The market for health care is characterized by information asymmetry, as patients delegate decision-making and rely on

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providers to select as well as administer treatment (Arrow, 1963). The performance of providers in low-and-middle-income countries continues to be scrutinized and there is widespread interest in strategies to improve their practice (Rowe, de Savigny, Lanata, & Victora, 2005). In designing interventions to improve the quality of care it is important to understand what or who influences providers' treatment decisions. Structural factors are often emphasized, and providers' practice may be constrained by the availability of essential equipment, supplies and medicines (Peabody, Taguiwalo, Robalino, & Frenk, 2006), and by shortages of health professionals, as existing staff care for large volumes of patients and substitute for more senior cadres (Chen et al., 2004). There is,

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however, evidence on providers' knowledge, competence and practice demonstrating that poor resource availability and knowledge of clinical guidelines are not the only reasons why patients receive poor quality care (Das, Hammer, & Leonard, 2008; Willis-Shattuck et al., 2008).

The literature on medical practice variation examines the extent to which individual providers affect the quality of patient care. The notion of 'practice style' was introduced to describe the variation attributed to providers' preference over alternative forms of care (Wennberg, Barnes, & Zubkoff, 1982). Early studies focused on geographic variation, and showed that variations in medical practice were not fully explained by patients' health care needs and demographic characteristics (McPherson, Wennberg, Hovind, & Clifford, 1982). As the literature grew, studies investigated differences between facilities and between individual providers (Scott & Shiell, 1997a, 1997b). For example, Davis et al. examined decision-making in primary care facilities and found considerable variation between doctors in prescribing, referral for diagnostic tests and follow up having accounted for case-mix, patient, and practitioner attributes (Davis, Gribben, Scott, & Lay-Yee, 2000). Although the literature on medical practice variation is reasonably extensive, it offers limited insight into the extent to which providers' preference varies by type of organization. Moreover, most studies come from high-income countries where facilities are well-resourced and institutions monitor and regulate the quality of health care.

Providers' preference over alternative treatments is said to be revealed by their actual practice, though the choice of treatment may be constrained by other factors, such as the stock of medicines. specific information about the patient's condition or the patient's ability to pay. Stated preferences are usually used in economic studies to substitute for revealed preferences under conditions where it is not possible to capture revealed preferences (because, for example, the product in question is not available in the market). However, in some cases it may be useful to focus on stated preferences in their own right, as distinct from revealed preferences. For instance, focussing on what providers' state they prefer, rather than what they know or do, will help to determine whether an intervention that targets providers' knowledge is likely to be effective or whether additional effort is needed to change what they prefer. In other words, it is acknowledged that changing what providers prefer may not be sufficient to change actual practice, but any gap between stated and revealed preference would require supplementary interventions, such as those that address resource constraints or reduce the patients' cost of accessing care.

Providers' stated preferences for the treatment of uncomplicated malaria were examined as part of the formative stages of a study undertaken to test supply-side interventions to improve malaria diagnosis and treatment in Cameroon and Nigeria (Wiseman, Ezeoke, et al., 2012; Wiseman, Mangham, et al., 2012). Malaria places a considerable burden on the health system in sub-Saharan Africa, and is treated by providers working at a range of facilities, including private-sector pharmacies and drug stores. The clinical guidelines for malaria treatment are unambiguous, and can be used by providers with limited clinical knowledge or expertise. Artemisinin-combination therapy (ACT) is the recommended antimalarial for uncomplicated malaria and should be supplied to all patients presenting with a fever or history of fever, unless they have a negative test result or are in the first trimester of pregnancy. ACT has been the first-line antimalarial in Cameroon since 2004 and in Nigeria since 2005. In each country, the Malaria Control Programme of the Ministry of Health, at either national or state level, is responsible for disseminating malaria policy (Ministry of Health of the Federal Republic of Nigeria, 2005; Ministry of Public Health of the Republic of Cameroon, 2008). Their efforts include

distributing clinical guidelines and holding training workshops. Providers in public and mission facilities have greater access to information and training, though professional associations may conduct training for staff at private-sector pharmacies and drug stores.

In this paper, we report the type of antimalarial that providers in Cameroon and Nigeria state they prefer to use to treat uncomplicated malaria. We assess whether their stated preference is consistent with their knowledge of the recommended antimalarial, and investigate who or what influences their preference over alternative antimalarials. Previous epidemiological studies from Cameroon and Nigeria have investigated the factors associated with patients receiving an ACT, though these studies do not focus on providers' preference or practice as they include patients at pharmacies and drug stores that requested specific treatment (Mangham et al., 2012, 2011). Studies from elsewhere in sub-Saharan Africa have examined providers' actual practice in treating febrile patients, though these were limited to care provided at public and mission facilities (Osterholt et al., 2006; Rowe et al., 2000; Zurovac et al., 2004). This paper complements the existing literature by investigating providers' preference using stated preference data obtained from providers working at non-profit health facilities and for-profit pharmacies and drug stores in Cameroon and Nigeria.

Theoretical considerations

Providers' preference over different types of antimalarials was examined from an economic perspective founded in agency theory. An agency relationship occurs when one individual acts on behalf of another (Shapiro, 2005), and this arises in health care interactions, including those at pharmacies and drug stores, when the patient relies on the provider to determine their health care needs (Coast, 2001). It is conventional to focus on the principal-agent relationship between patients and providers, though providers may be party to multiple agency relationships (Blomqvist, 1991). In this study, we acknowledge that providers operate within a network of relationships, and may be an agent not only for their patients but also for other actors in the health system, such as their employer, the Ministry of Health, or antimalarial supplier (Jan, 2005). Agency relationships may have a formal contract, though will often be an unwritten understanding in which the provider perceives a responsibility to act on behalf of another.

The economics literature assumes agents are rational and make choices to maximize their own utility. In standard agency theory it is assumed that agents are financially motivated and would act to obtain an optimal combination of income and leisure time, or at least achieve a threshold level of income, irrespective of the principal's preference (Evans, 1974). The provider's preferred treatment could, therefore, reflect the method of remuneration, whether the organization has a profit motive, or income from additional sources, such as secondary employment, sales commission, or ownership of private businesses (Chaix-Couturier, Durand-Zaleski, Jolly, & Durieux, 2000; Ferrinho, Van Lerberghe, Fronteria, Hipolito, & Biscaia, 2004). These influences can be considered from a static or dynamic perspective, with the latter taking into account reputation effects, in which future income depends on the amount of competition and the principal's satisfaction with the agent's current practice (Mooney & Ryan, 1993). The theory has also been extended to recognize that providers have a professional responsibility to act in the interests of the patient and may derive satisfaction from their work (Mooney & Ryan, 1993). Thus, providers' choice of treatment may reflect an intrinsic motivation not only to fulfil patients' expectations and improve patients' health, but also to satisfy their employer, the Ministry of Health or other principals (Leonard & Masatu, 2010).

Agents' choice, and therefore their ability to obtain utility, will be constrained by the information they have available. Providers may vary in their access to information from pre- or in-service training, clinical guidelines, public health campaigns, marketing materials, and observing colleagues. Institutional, social and psychological factors may also constrain preferences. Formal institutions, such as regulation, can limit behaviour, though informal institutions can also have an important effect, as preferences are embedded within social structures, cultures, values and behavioural norms (Burke, Fournier, & Prasad, 2010; Charles, Gafni, Whelan, & O'Brien, 2006; Rabin, 1998). For instance, providers may be influenced by their colleagues, as social networks not only affect the flow of information but can be a source of reward and punishment (Granovetter, 2005).

Methods

Econometric model

The econometric analysis is based on random utility theory. Although utility cannot be directly observed, individuals are assumed to be economically rational and make choices that maximize their utility. The provider's choice of preferred treatment can be described as:

U = f(Y, S)

where *U* is the utility of the provider's preferred treatment, *Y* is income (and other financial incentives), *S* is the satisfaction (and non-financial incentives). Utility is maximized subject to the information about the treatment options and the underlying institutional environment. It is assumed that the utility yielded by mutually exclusive treatment options depends on the observable factors contained in the provider's utility function and unobserved or unknown influences on individual behaviour. In its simplest form, the observed sources of utility are defined as a linear expression in which each explanatory variable is weighted by a parameter that accounts for that variable's marginal utility.

A multilevel model was used to estimate a three-level random effects model (Hox, 2010). This approach accounts for the clustering of providers, since some correlation between providers within a facility or area is possible if they have similar incentives, share information, and face a common institutional environment (Rice & Jones, 1997). For a three-level logistic regression the dependent variable π_{ijk} is defined as the probability that the preferred treatment was an ACT for provider *i* from facility *j* in area *k*, where (π_{ijk} /(1- π_{ijk})) is the log odds that the preferred treatment is an ACT. The model for provider's preferred treatment is specified as:

$$logit(\pi_{ijk}) = \alpha + \beta Y_{ijk} + \lambda S_{ijk} + \theta I_{ijk} + \gamma F_{jk} + \phi A_k + \varepsilon_{ijk} + u_{jk} + \nu_k$$

$$\varepsilon_{ijk} \sim N(0,\sigma^2) \rightarrow u_{jk} \sim N(0,\tau^2), v_k \sim N(0,\varphi^2),$$

where:

 α is the intercept;

 Y_{ijk} is the income of provider *i* at facility *j* in area *k*; S_{ijk} is satisfaction of provider *i* at facility *j* in area *k*; I_{iik} are information constraints for provider *i* at facility *j* in area *k*; F_{jk} are institutional constraints common to all providers at facility *j* in area *k*;

 A_k are institutional constraints common to all providers in area k;

 β , λ , θ , γ and ϕ are the parameters associated with the explanatory variables;

 ε_{ijk} , u_{jk} and v_k , are the residuals at the level of the provider, facility and geographical area, respectively, and capture unobserved variation, measurement and specification errors.

Study setting

The study was undertaken in four sites in Cameroon and Nigeria that had been selected for cluster randomized trials of interventions to support the introduction of malaria rapid diagnostic testing (Wiseman, Ezeoke, et al., 2012; Wiseman, Mangham, et al., 2012). This paper analyses provider survey data that were collected as part of a larger study on malaria diagnosis and treatment at different types of facility and undertaken to guide the design of interventions that would accompany the roll-out of malaria rapid diagnostic tests.

The four sites were Yaoundé and Bamenda in Cameroon, and Enugu and Udi in Enugu State, south-east Nigeria. Yaoundé is the capital of Cameroon and has an urban, predominately Frenchspeaking population. The Bamenda site consisted of one urban and seven rural districts in the North-West region, where the main language is English or pidgin-English. The urban sites in Nigeria were drawn from Enugu town, and the rural areas were located in Udi local government area. Igbo is the dominant ethnic group and language in Enugu State. Malaria is endemic and occurs throughout the year in all four sites, though there is seasonal variation in the Bamenda site, with peak transmission occurring between March and November.

Antimalarials, including ACT, have over-the-counter status in Cameroon and Nigeria and can be obtained from pharmacies and drug stores as well as public, mission and private facilities. Malaria treatment may also be sought from mobile medicine vendors, herbalists and traditional healers. The government supplies public facilities, and mission facilities receive medicines from a central agency. Pharmacies and drug stores obtain medicines through formal and informal channels, including drug company representatives, wholesalers and the main market in the local area.

In Cameroon, public and mission facilities, and private pharmacies are the main source of treatment for uncomplicated malaria (Ongolo-Zogo & Bonono, 2010). Most public and mission hospitals and health centres in the Cameroon sites have a pharmacy and a laboratory for simple diagnostic procedures and are staffed by nurses, pharmacy attendants and laboratory technicians. Some larger facilities also have a medical doctor. In the private-sector, pharmacies are legally required to employ a qualified pharmacist and licensed to sell prescription and over-the-counter medicines. In addition, antimalarials are available at drug stores in the North-West region, which are typically owned and staffed by providers with no or few qualifications (Reynolds Whyte, van der Geest, & Hardon, 2002). In Enugu State, Nigeria, treatment for uncomplicated malaria is most frequently obtained at public health centres, pharmacies and drug stores (known as patent medicine stores) (Onwujekwe et al., 2005). Malaria diagnostic testing is not widely available at the primary care level and public facilities are staffed by nurses, community health officers and extension workers. Forprofit pharmacies and drug stores are formally recognised in the health system and have professional associations. Licensed pharmacies are required to have a qualified pharmacist, while patent medicine dealers are not required to have specific qualifications or training (Okeke, Uzochukwu, & Okafor, 2006) and are formally restricted from selling prescription-only medicine.

Survey data

Data on providers' stated preference for treating uncomplicated malaria were obtained in stratified multi-stage cluster surveys conducted at selected facilities in the study sites between July and December 2009 (Mangham et al., 2012, 2011). The sampling of geographic areas and facilities was undertaken separately for each country, based on an enumeration of facilities conducted in March-May 2009. At selected facilities a patient exit survey, a provider survey and a facility audit were conducted. Sample size calculations were undertaken for the patient exit survey and sought to determine the proportion of patients supplied ACT, with a given level of precision (Mangham et al., 2012, 2011). The primary outcome was the proportion of individuals reporting seeking treatment for a fever that were supplied (prescribed or received) an ACT. In Cameroon a survey sample of 12 patients per public facility was calculated to estimate the primary outcome with a prevision of +/-8.6%, and eight patients per mission facility and medicine retailer

Table 1

Dependent and explanatory variables.

| Variable | Coding | Proportion |
|---------------------------------------|-----------------------------|------------|
| Variable | county | rioportion |
| Dependent | | |
| Stated Preference: ACI is best | Yes (1) | 0.69 |
| type of AM for | No (0) | |
| uncomplicated malaria | | |
| Explanatory | | |
| Level 1. Provider $(N = 518)$ | Fixed Salamy employees (1) | 0.91 |
| Remuneration method. | Fixed Salary employee (1) | 0.81 |
| | Sales-felaleu as | |
| Works at other facilities: | Voc (1) | 0.02 |
| works at other facilities. | $N_{\rm e}(0)$ | 0.05 |
| Reports patients usually ask for ACT | NO(0) | 0.52 |
| Reports patients usually ask for ACT. | No(0) | 0.52 |
| Knows ACT is recommended: | Vec (1) | 0.61 |
| Kilows Act is recommended. | No(0) | 0.01 |
| Has access to guidelines: | Vec(1) | 0.28 |
| Thas access to guidelines. | No(0) | 0.28 |
| Attended malaria training | Ves (1) | 0.36 |
| in past 3 years. | No (0) | 0.50 |
| Cadre: | Doctor (1) | 0.06 |
| caure. | Nurse or Midwife (2) | 0.16 |
| | Nurse Assistant (3) | 0.05 |
| | Health Extension Worker (4) | 0.16 |
| | Pharmacy or laboratory | 0.18 |
| | technician (5) | 0110 |
| | No formal gualifications | 0.37 |
| | (PMD or attendant) (0) | |
| Years worked at facility: | <1vear (0) | 0.18 |
| 5 | 1-4 years (1) | 0.34 |
| | 5–10 years (2) | 0.32 |
| | 11 + years(3) | 0.16 |
| Level 2: Facility ($N = 245$) | 2 | |
| Facility Ownership: | Non-profit Public/ | 0.46 |
| | Mission (1) | |
| | Private-for-profit | |
| | Drug Retailer (0) | |
| AM supplied by drug | Yes (1) | 0.10 |
| company representative | No (0) | |
| Level 3: Area $(N = 36)$ | | |
| Density of facilities: | Low (<10 per area) (0) | 0.22 |
| | Medium (10–19 per | 0.37 |
| | area) (1) | |
| | High $(20 + per area)(2)$ | 0.41 |
| Residence | Urban (1) | 0.72 |
| | Rural (0) | |
| Country: | Cameroon (1) | 0.71 |
| | Nigeria (0) | |

was calculated to estimate the primary outcome with a precision of +/- 6.2% (Mangham et al. 2012). In Nigeria, a survey sample of 20 patients per public facility was calculated to estimate the primary outcome with a precision of +/- 13%, while 14 patients per medicine retailer allows the primary outcome to be calculated with a precision of +/- 6.6% (Mangham et al. 2011). All of these calculations assume the intra-cluster correlation in treatment between facilities was 0.3. These precision estimates differ given the different sample sizes per type of facility and assume a prevalence of 50% for the primary outcome.

In each country, geographic areas were randomly selected, stratified by site. Facilities dispensing antimalarials were then selected based on the number and distribution of facilities in each area. In both countries, all public primary care facilities were included and pharmacies and drug stores were randomly selected with probability proportionate to their number in the local area. In Cameroon, all district hospitals and mission facilities in the selected areas were also included since they were an important source of treatment in Yaoundé and Bamenda (though not a major source of treatment in the Nigerian study sites). The provider survey was undertaken at all facilities selected for the patient exit survey and individually administered by trained fieldworkers to all providers that prescribe or dispense medicines, were available at the time of the survey and gave informed consent. Most facilities had two or three providers who prescribed or dispensed treatment, though the number ranged from one to twelve. In addition, one provider in each facility completed the facility survey.

Provider and facility questionnaires were administered to obtain data on provider and facility characteristics, and the health care available for febrile illness. Providers were asked about their preservice and in-service training, access to guidelines, knowledge of recommended treatment, and preference over different antimalarials. Providers were asked to state their preference over alternative antimalarials prior to questions on training, guidelines and malaria treatment policy to avoid framing bias that could arise by referring first to the recommended antimalarial. The questionnaires were developed specifically for the study and pre-tested at facilities not selected for the survey. Site co-ordinators monitored and supervised data collection. Data were independently doubleentered and verified using Microsoft Access 2007 (Microsoft Inc., Redmond, Washington). Data entry errors were corrected to ensure consistency with the original form.

Dependent and explanatory variables

The dependent variable was a binary outcome derived from the question "which antimalarial do you think is the best for treating patients with uncomplicated malaria?". Providers could respond by stating a generic or brand name. Each response was recorded and subsequently coded: ACT, artemisinin-monotherapy, chloroquine, sulphadoxine-pyrimethamine, quinine, other, and don't know. No provider refused to answer this question. The dependent variable was 1 if the provider responded ACT and 0 otherwise.

Explanatory variables occurred at three levels (Table 1). Provider attributes were at level-1, and included the method of remuneration, based on whether the individual was the owner or an employee. As providers may yield income from patients obtaining treatment at a private facility, a variable was included for whether providers work elsewhere, though we recognized providers may be unwilling to disclose information relating to their financial interests. A binary variable was used to identify providers who reported their patients usually ask for an ACT since providers may derive satisfaction from fulfilling patient expectations. Several variables indicated providers' information about ACT, including whether or not the provider knew ACT was recommended by the government, had access to a copy of the malaria treatment guidelines, and attended malaria training in the past three years. Providers' cadre was included since pre-service training may have affected the information they had available, and we controlled for the number of years worked at a facility.

At the facility level (level-2), a variable indicated whether providers work in a non-profit organization (owned by the government or mission) or in a private-for-profit organization. Facility ownership may affect the income incentive of providers, or their employers, though may also reflect differences in the information available and the institutional environment. Whether a facility received antimalarials from drug company representatives was also included since they may use financial incentives, such as discounts or commission, to encourage the sale of specific products, as well as share information and promotional materials on their products. It was expected that drug company representatives would promote ACT over other types of antimalarials.

Area-level (level-3) variables included whether the provider worked in an urban or rural setting, the density of health facilities in the locality, and the country. Random effects were used to capture the degree to which providers' preference were clustered since it was hypothesized that providers working within the same facility may have similar preferences because they operate within the same institutional context, share information, learn from others and conform to social norms. Providers' social network may also extend to others working in the local area, and for the same reasons may have similar preferences over different treatments.

Empirical strategy

The first step was to analyze stated preference using an intercept-only model in order to determine the suitability of a multilevel model over a single-level model and whether to adopt two or three levels (Hox, 2010). Likelihood ratio tests were used to compare model fit. The proportion of the total variance that was attributable to each level of the model was estimated using the variance partition coefficient (VPC). The VPC is similar to the intracluster correlation, though used when the dependent variable is discrete. The VPC was calculated as:

$$VPC_{facility} = \left(\sigma_{facility}^2 / \sigma_{facility}^2 + \sigma_{area}^2 + 3.29\right)$$

and

$$VPC_{area} = \left(\sigma_{area}^2 / \sigma_{facility}^2 + \sigma_{area}^2 + 3.29\right)$$

where the variance at level 1 was the variance of the standard logistic distribution ($\pi^2/3 = 3.29$) (Hox, 2010). Larger values of the VPC (0 < VPC < 1) indicate greater potential for a level to influence the value of the dependent variable.

The second step was to estimate a random-intercept model with all explanatory variables at provider, facility and area levels that were hypothesized may influence providers' preference over alternative antimalarials. The VPC showed the proportion of the total variance attributable to each level that remained having incorporated explanatory variables. The third step was to examine the random-intercept model with interaction terms. Interactions were investigated for combinations of explanatory variables for which it was hypothesized there may be a joint effect. Interactions between facility ownership and information variables were examined since access to guidelines and training may depend on the type of facility. Access to guidelines, attendance at training, cadre, and whether supplies were received from drug company representatives were each interacted with knowledge that ACT was the recommended treatment. Finally, interactions were used to investigate whether provider, facility and area characteristics have a country-specific effect. Interactions were added to the randomintercept model one at a time. The statistical significance was assessed using the Wald test and the likelihood ratio test. Interaction terms were retained in the model if they were significant at the 10% level.

Multilevel models were estimated using adaptive quadrature to approximate the marginal likelihood by numerical integration in Stata 11.2 (StataCorp, 2009). Although computationally demanding, estimation with numerical integration was the preferred method as there were small cluster sizes at level-2 and quasi-likelihood methods would be susceptible to bias (Hox, 2010; Rodriguez & Goldman, 1995). Bootstrap and Bayesian methods are also recommended for small cluster sizes (Hox, 2010), though numerical integration was used as it is well-suited for relatively simple models with binary outcomes (Steele, 2009). Model stability was assessed by comparing the model estimates from adaptive quadrature with seven integration points, with those generated by a model using a higher number of integration points.

Several methods were used to assess model specification. The assumption of normally distributed residuals was examined using normal plots of standardized level-2 and level-3 residuals. Multicollinearity was assessed using the variance inflation factor, since large inflation factors show evidence of correlation among explanatory variables. The deviance, which equals minus two times the log likelihood, was reported and is an indication of goodness of fit. The Ramsev RESET test was also used as this is a general test for problems associated with the functional form (Jones, 2007). It involves taking the square of the predicted value and re-estimating the model with this as an additional explanatory variable. If the model is well specified the new variable will not be significant (Rice, 2000). The RESET test can, therefore, identity specification errors associated with omitted variable bias, simultaneity bias or measurement error if they lead to nonlinearity in the relationship between the dependent and explanatory variables. Finally, the model was estimated with and without the explanatory variable for knowing ACT was recommended to investigate the simultaneity bias that would arise if providers' preference over alternative antimalarials was determined at the same time they acquired knowledge of the recommended treatment.

The final results were validated by re-analysing the final model using Bayesian Markov Chain Monte Carlo (MCMC) estimation methods in MLwiN 2.25 (Rasbash, Charlton, Browne, Healy, & Cameron, 2012). The MCMC estimation used uninformative priors and starting values based on second-order penalized quasilikelihood (PQL2) generated using restricted iterative generalized least-squares (RIGLS) (Browne, 2012). Convergence of the Markov chain was assessed graphically and by checking that similar posterior distribution summaries were achieved with different starting values. Again, goodness of fit was assessed using the RESET Test.

Results

The study was based on a population of 518 providers working at 245 facilities in 36 geographic areas in Cameroon and Nigeria. Of the 540 providers invited to participate in the survey, 9 refused to give consent, and 13 had missing data for at least one of the model variables. The analysis was conducted on complete cases as bias from missing responses was expected to be small.

The study population included 240 providers from public and mission facilities and 278 providers from pharmacies and drug stores, with providers in Cameroon representing 71% of the study population (Table 1). The majority (81%) of providers were employees and less than 3% reported working at other facilities. Just

over half (52%) of the providers reported ACT was the antimalarial most often requested by patients. Almost two-thirds (61%) of providers stated ACT was the antimalarial recommended by the government, though only 36% of providers attended malaria training in the past 3 years, and 28% of providers had access to a copy of the national malaria treatment guidelines. The providers spanned a range of cadres, though the largest group (37%) were patent medicine dealers and sales attendants without formal health qualifications. The length of time providers had worked at the current facility ranged from less than one year to more than 11 years.

Overall 69% (359/518) of providers stated ACT was the best treatment for uncomplicated malaria. Other responses included quinine and artemisinin-monotherapy, which are recommended for severe cases of malaria, and sulphadoxine-pyrimethamine, which was the former first-line therapy (Table 2).

Table 3 presents the two-way relationship between providers' stated preference and their knowledge of the antimalarial recommended by the government for uncomplicated malaria. Overall, 46% (236/518) of all providers surveyed reported ACT was their preferred treatment and knew it was recommended. There were 24% (123/518) of providers who stated a preference for ACT and did not know it was the recommended treatment, but also 16% (82/518) of providers who knew ACT was the recommended treatment and did not report this was the best treatment.

The degree of variability in providers' preference that can be attributed to facility and area levels was examined using interceptonly models to determine whether to use a two-level and threelevel logistic regression. Significant random effects were found at both levels, and the deviance and likelihood ratio tests indicate that the three-level model (Model 1 in Table 4) was superior to the twolevel models (Appendix A).

The odds ratios generated by the three-level logistic regression containing explanatory variables are presented in Table 4. Model 2 included all explanatory variables except the variable "Knows ACT is the recommended treatment", while Model 3 included all explanatory variables. As expected, the introduction of the explanatory variables reduced the residual variability within facilities and areas (compared to Model 1). Model estimates were stable to three decimal places. The RESET test indicated Models 2 and 3 were well specified and there was no evidence of multicollinearity or simultaneity bias. Model 3 was preferred, based on model diagnostics, and was used to investigate interaction terms, though none were found to significantly improve the fit of the model.

The final model (Model 3) showed that providers' stated preference for an ACT was not significantly associated with income incentives, as measured by the method of remuneration and whether they worked elsewhere. Providers were, however, twice as likely to state a preference for ACT if this was the type of antimalarial most often requested by their patients. Knowing ACT was the recommended treatment was also a significant determinant, with the odds of stating a preference for ACT 2.5 times greater amongst Table 3

Two-way relationship between knowledge of guidelines and preference for ACT.

| | | Stated ACT was the best treatment for uncomplicated malaria | | | | | | |
|---------------------------|-------|---|------|-----|------|------------|-------|--|
| | | Yes | | No | | Total | | |
| | | N | % | N | % | N | % | |
| Knows ACT is | Yes | 236 | 45.6 | 82 | 15.8 | 318 | 61.4 | |
| for uncomplicated malaria | Total | 359 | 69.3 | 159 | 30.7 | 200 518 | 100.0 | |

providers who reported ACT was recommended by the government. The results also showed the effect of malaria training was of borderline significance, and access to malaria treatment guidelines did not significantly predict a preference for ACT. Providers' preference for ACT was significantly lower at non-profit facilities, and the odds of preferring an ACT was 4 times greater if the facility obtained antimalarials from drug company representatives. Random effects remained relatively large after the inclusion of explanatory variables indicating there was unexplained variability attributable to the facility and local area.

The sensitivity of the results to the estimation method was investigated by reanalysing the final model in MLwiN 2.25 using PQL2 generated using RIGLS and then by running Bayesian MCMC using non-informative priors. The results were similar and are provided in Appendix B.

Discussion

The majority of providers stated a preference over different types of antimalarials, with just 8% unable or unwilling to state which antimalarial they prefer for treating uncomplicated malaria. 69% of providers had a preference for ACT, though alternatives included quinine and artemisinin-monotherapy, which should be reserved for cases of severe malaria, and sulphadoxinepyrimethamine, which was the former first-line treatment.

Method of remuneration, access to additional employment income, and facility ownership were used as proxies to investigate the effect of financial incentives on providers' preference. Of these variables, facility ownership had a significant effect, with providers at for-profit facilities more likely to prefer an ACT over other antimalarials. Further research would be required, however, to ascertain whether the effect of facility ownership reflects income incentives or other institutional characteristics.

We found a positive association between providers who stated a preference for ACT and providers who reported ACT was the antimalarial their patients most often request. This suggests that providers were more likely to prefer ACT if their patients prefer (or perceive their patients prefer) ACT, though the interpretation is

| Table | 2 |
|-------|---|
|-------|---|

Providers' stated preference for treatment of uncomplicated malaria.

| | Country | | | | Type of facility | | | | All | |
|----------------------------|----------|------|---------|------|------------------|------|-------------------|------|---------|------|
| | Cameroon | | Nigeria | | Public/Mission | | Medicine retailer | | | |
| | N = 369 | % | N = 149 | % | N = 240 | % | N = 278 | % | N = 518 | % |
| ACT | 266 | 72.1 | 93 | 62.4 | 156 | 65.0 | 203 | 73.0 | 359 | 69.3 |
| Artemisinin monotherapy | 2 | 0.5 | 23 | 15.4 | 7 | 2.9 | 18 | 6.5 | 25 | 4.8 |
| Chloroquine | 0 | 0.0 | 10 | 6.7 | 8 | 3.3 | 2 | 0.7 | 10 | 1.9 |
| Quinine | 63 | 17.1 | 0 | 0 | 44 | 18.3 | 19 | 6.9 | 63 | 12.2 |
| Sulphadoxine-pyrimethamine | 1 | 0.3 | 17 | 11.4 | 7 | 2.9 | 11 | 4.0 | 18 | 3.5 |
| Other AM | 0 | 0.0 | 4 | 2.7 | 2 | 0.8 | 2 | 0.7 | 4 | 0.8 |
| No preference | 37 | 10.0 | 2 | 1.4 | 16 | 6.7 | 23 | 8.3 | 39 | 7.5 |

Table 4

Factors predicting providers' stated preference for ACT.

| Fixed effects | | MODEL 1: Interce | ept-only model | MODEL 2: With all explanatory variables except knowledge | | | MODEL 3: With all explanatory variables | | |
|--------------------------------|--------------------------|------------------|----------------|--|-------------|---------|---|-------------|---------|
| | | | | OR | SE | P-value | OR | SE | P-value |
| Level 1: Provider | _ | | | | | | | | |
| Remuneration method: | Fixed salary | | | 1.46 | 0.712 | 0.434 | 1.63 | 0.794 | 0.320 |
| | Sales related | | | Ref | | | Ref | | |
| Additional employment: | Yes | | | 1.94 | 1.928 | 0.507 | 2.04 | 2.054 | 0.477 |
| | No | | | Ref | | | Ref | | |
| Reports patients usually | Yes | | | 2.17 | 0.737 | 0.023 | 2.08 | 0.710 | 0.033 |
| ask for ACT: | No | | | Ref | | | Ref | | |
| Has access to guidelines: | Yes | | | 2.06 | 0.901 | 0.100 | 2.04 | 0.900 | 0.106 |
| | No | | | Ref | | | Ref | | |
| Has attended malaria training: | Yes | | | 1.96 | 0.662 | 0.047 | 1.88 | 0.638 | 0.061 |
| | No | | | Ref | | | Ref | | |
| Knows ACT is recommended: | Yes | | | _ | - | - | 2.54 | 0.824 | 0.004 |
| | No | | | | | | Ref | | |
| Cadre: | Doctor | | | 1.18 | 0.907 | 0.127 | 0.79 | 0.613 | 0.147 |
| | Nurse or Midwife | | | 2.21 | 1.308 | | 1.96 | 1.160 | |
| | Nurse Assistant | | | 1.37 | 1.047 | | 1.16 | 0.888 | |
| | Extension Worker | | | 0.72 | 0.392 | | 0.61 | 0.336 | |
| | Pharmacist/technician | | | 0.58 | 0.296 | | 0.55 | 0.281 | |
| | No qualifications | | | Ref | | | Ref | | |
| Years worked at facility: | <1 year | | | Ref | | 0.440 | Ref | | 0.406 |
| | 1—4 years | | | 0.81 | 0.373 | | 0.74 | 0.346 | |
| | 5—10 years | | | 0.53 | 0.257 | | 0.50 | 0.241 | |
| | 11 + years | | | 0.95 | 0.555 | | 0.88 | 0.517 | |
| Level 2: Facility | | | | | | | | | |
| Ownership: | Public/Mission | | | 0.40 | 0.248 | 0.140 | 0.33 | 0.205 | 0.075 |
| | Drug Retailer | | | Ref | 1050 | 0.007 | Ref | 4.0.40 | 0.000 |
| AM supplied by drug | Yes | | | 5.77 | 4.858 | 0.037 | 4.83 | 4.048 | 0.060 |
| company rep | NO | | | Ref | | | Ref | | |
| Level 3: Area | T | | | D-f | | 0.000 | Def | | 0.072 |
| Density of facilities: | LOW | | | Ker 0.00 | 0.000 | 0.809 | Ker | 0.700 | 0.872 |
| | Medium | | | 0.99 | 0.800 | | 0.97 | 0.798 | |
| Pasidonso | High | | | 1.58 | 1.514 | 0 702 | 1.43 | 1.397 | 0.666 |
| Residence | DiDdii | | | 1.24 Rof | 1.050 | 0.795 | 1.44 Dof | 1.225 | 0.000 |
| Country | Kuldi | | | 1.00 | 1 201 | 0.202 | 1.01 | 1 100 | 0.266 |
| Country | Vigoria | | | 1.99 Ref | 1,201 | 0.265 | 1.01 Dof | 1.100 | 0.500 |
| Pandom Effects | Nigelia | Ectimato | SE. | Ectimato | CE | | Estimato | SE. | |
| Random Ejjetis | Level $2r^2(n)$ | | 3E 1 334 | | 3E 1 206 | | 2 49C | 3E 1 170 | |
| Residual vallance | Level-2: $\sigma^2(u_j)$ | 2.54 | 0.862 | 1 20 | 0.768 | | 2.400 | 0.817 | |
| VPC | Level-2: facility | 0.377 | 0.002 | 0.366 | 0.700 | | 0.345 | 0.017 | |
| vi C. | Level_3: area | 0.209 | | 0.300 | | | 0.198 | | |
| Diagnostics | LEVEI-J, alea | 0.203 | | 0.175 | | | 0.150 | | |
| Deviance (-2^*llh) | | 577 074 | | 536 568 | | | 527 868 | | |
| RESET | | _ | | 0 249 | | | 0.278 | | |
| | | | | 5.2 15 | | | 5.270 | | |

uncertain. For example, providers may derive utility from selecting ACT, either because they have an intrinsic motivation to satisfy their patients, or because they want to maintain a good reputation and secure future income. Local competition would also be expected to affect the latter, though there was no evidence that the density of facilities within an area had an effect on providers' preference. Alternatively, it could be argued that the association reflects an omitted exogenous factor, such as a public health campaign, that had an influence on both providers' and patients' preference. Either way, knowing that preferences were positively associated may be useful for designing strategies to improve providers' practice or influence patients' demand.

It was encouraging, and not unexpected, to find providers who knew ACT was the recommended treatment for uncomplicated malaria were significantly more likely to state a preference for ACT. Moreover, providers that had attended malaria training in the past three years were more likely to state a preference for ACT (at the 10% level of significance) having controlled for their knowledge. This suggests training can have an effect that goes beyond informing providers about treatment policy and can influence their preferences over different treatments. Access to malaria treatment guidelines had no significant effect on providers' preference, even in the model which did not control for their knowledge. This suggests having access to guidelines is not a good predictor that providers will supply the recommended treatment. The results imply, therefore, that the nature of communication can have an important influence on providers' preference and further research on this may help to identify effective strategies for educating providers about changes in health policy and clinical guidelines.

The results suggest an agency relationship in which drug company representatives (drug reps) influence providers' preference over antimalarials, though it is also possible that obtaining medicines from drug reps may proxy for unobserved organizational attributes. If there is a direct effect, then this could reflect explicit incentives, such as sales commission, or an information effect from marketing strategies that promote the use of ACT. The interaction between knowledge that ACT is recommended by the government and use of drug reps did not significantly improve the model, which suggests drug reps have an effect that is independent of providers' knowledge of the recommended treatment, though the sample from which to detect interaction effects was limited. In any case, there may be merit in exploring the potential to engage drugs reps in strategies to change providers' preference and improve their practice. There are few examples in the empirical literature, though a vendor-to-vendor education programme in Kenya, in which wholesalers were trained to supply providers at drug shops and kiosks with information and job aids on malaria treatment, was found to have a moderate effect (Tavrow, Shabahang, & Makama, 2003).

There is evidence that providers' preference for ACT was similar among colleagues within a facility and among providers within a local area. Although the level-2 and level-3 residual variance was reduced by the inclusion of explanatory variables, it remained significant in the final model and the VPC indicated that a substantial proportion of the unexplained heterogeneity can be attributed to facility and area factors. This may reflect the influence of institutional and behavioural factors, such as networks and social norms, though we are cautious in drawing conclusions since average cluster size was small and the size of the random effect depends on the estimation method. Further research would be beneficial to explore how preferences may be shaped or constrained by colleagues, and how strategies to improve providers' practice could utilize networks or promote social norms.

There are some methodological limitations to our work. First, there is uncertainty in how providers understood the question used to elicit their preference over alternative antimalarials. The question "which antimalarial do you think is best for treating uncomplicated malaria?" followed questions on the type of antimalarial usually supplied and type of antimalarial patients' prefer. It is possible, however, that some providers understood the question to be asking about the efficacy of different antimalarials, or aspects of the treatment regimen, such as the number of tablets, or potential side effects. If this were the case, then we would expect the effect of income and satisfaction on their choice of treatment to be reduced as providers focus on other attributes. Qualitative methods may be useful to probe what providers understand by 'best' in this context. Moreover, it is possible that our direct method of eliciting stated preference encouraged providers to give a socially acceptable response and report what they know is recommended. More sophisticated methods, such as discrete choice experiments, are often used and designed to overcome this framing bias. The direct method was, however, practical given that the formative research sought to examine multiple questions about the treatment of uncomplicated malaria, and was also feasible since ACT was not a new product.

Second, the sample size was restricted because the provider survey was conducted as part of a larger study principally designed to examine the treatment supplied to febrile patients. None of the interactions included in the model were found to have a significant effect, and this may be due to the limited number of observations. Furthermore, the average cluster size at level-2 was small since the survey involved many primary care facilities and medicine retailers that operate with few, sometimes lone, providers. In this setting, the small cluster sizes could not have been overcome and they were an important consideration for the statistical analysis. Correlation between providers within a facility was empirically investigated to determine whether facility should be included as a level in the model. There remained evidence of clustering at the facility-level (as well as the area-level) once explanatory variables were added to the model. In addition, the robustness of the study results to the estimation method was investigated because of the small cluster sizes at the facility-level. The alternative methods generated comparable results, though the small cluster sizes may have explained the differences in the magnitude of estimated coefficients. This is consistent with findings from a recent study which showed how the choice of estimation method and software can affect the results of multilevel logistic regression when the data are limited and the average cluster size is small (Li, Lingsma, Steyerberg, & Lesaffre, 2011).

Conclusions

Ensuring providers prefer to supply the recommended type of antimalarial is an important prerequisite for ensuring patients with uncomplicated malaria receive the most effective treatment. Providers were asked which antimalarial they think is the best for treating patients with uncomplicated malaria to elicit which antimalarial providers prefer to supply when not constrained by the resources available or patients' ability to pay, and we investigated who or what influences their preference. The type of antimalarial providers prefer not only depended on their knowledge of the clinical guidelines, but also reflected their perceptions of what patients prefer, and the influence of drug company representatives, their colleagues and other providers in the locality. These findings support the premise that providers are agents serving multiple principals. Understanding who and what influences providers' stated preference over alternative antimalarials is useful for identifying strategies to encourage providers to supply effective malaria treatment. The influence of multiple actors on the providers' choice of treatment emphasizes the need to communicate changes in drug policy not only to providers but also to suppliers and local communities. Moreover, our findings suggest that public health interventions would be more effective if they target groups of providers, rather than individuals, and promote a supportive environment since providers working within a facility or local area have similar preferences.

Ethical approval

Ethical approval was obtained from the ethics committees of the London School of Hygiene and Tropical Medicine (5429), University of Nigeria (03.11.08) and Cameroon National Ethics Committee (030/CNE/DNM/09).

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Appendix. Supplementary data

Supplementary data related to this article can be found at http:// dx.doi.org/10.1016/j.socscimed.2013.12.024

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