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How Much Malaria Occurs in Urban Luanda, Angola? A Health Facility-Based Assessment

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Abstract. We conducted a health facility-based survey of patients with fever during malaria transmission season to determine the proportion with laboratory-confirmed malaria in Luanda, Angola. We enrolled 864 patients at 30 facilities; each underwent a blood film for malaria and a questionnaire. Only 3.6% had a positive blood film. When stratified by distance of the facility to city center (< 15 km and ≥ 15 km), the proportions were 1.5% (9/615) and 8.8% (22/249), respectively ($P < 0.0001$). Of patients traveling outside Luanda in the preceding 3 months, 6.8% (6/88) had malaria, compared with 3.2% (26/776) not traveling ($P = 0.13$). Children < 5 years of age were less likely to have malaria (2.4%; 12/510) than children ages 5–14 (8.7%; 9/104) and adults (4.0%; 10/250) ($P = 0.03$). The prevalence of laboratory-confirmed malaria in febrile patients in Luanda is very low, but increases with distance from the urban center. Prevention and treatment should be focused in surrounding rural areas.

INTRODUCTION

Since 2000, the malaria control landscape has changed dramatically in Africa with the creation of the Global Fund to Fight acquired immunodeficiency syndrome (AIDS), Tuberculosis, and Malaria, the World Bank Malaria Booster Program, and the U.S. President's Malaria Initiative. For the first time, funding is now available to significantly reduce malaria morbidity and mortality in the most highly endemic areas of sub-Saharan Africa. Despite the substantial increase in funding, major gaps between needs and resources still exist. National Malaria Control Programs and their donor partners need to make the most cost-effective use of limited resources by targeting malaria control measures to those areas where they will have the greatest impact.

The city of Luanda, the capital of Angola, is home to an estimated 4.5 million people, or at least 25% of the country's total population of 16 to 17 million, and receives only 32 cm of rainfall annually, from February to April.[1] According to Ministry of Health statistics, Luanda province, which encompasses the capital city and surrounding rural areas, accounts for more cases of malaria than any other province, although most of these cases are clinically diagnosed and no information is available on where they were acquired. However, the 2006 Angola Malaria Indicator Survey found a low parasitemia prevalence of 5.5% among children < 5 years of age in Luanda province compared with 29.0% in surrounding rural provinces.[2] Furthermore, routine entomologic surveillance from January 2007 to January 2008 in 350 houses in Luanda found only 35 *Anophelines* during that period, in contrast to over 10,342 *Culicines* collected in the same locations (Burkot T, unpublished data). These data have cast doubts about the true burden of malaria in Luanda. If malaria has been overreported in the capital, then malaria treatment and control efforts there may have been diverting resources from rural areas where malaria transmission is generally higher.

Therefore, we conducted a health facility-based assessment of patients in Luanda city with fever or history of fever, including rapid diagnostic test (RDT), blood film, and questionnaire, to determine what proportion of patients with fever had laboratory-confirmed malaria, and what proportion of patients with laboratory-confirmed malaria had a history of recent travel outside Luanda.

MATERIALS

Our assessment methodology was based on the Rapid Urban Malaria Assessment (RUMA) protocol developed by Shr-Jie Wang and colleagues, with support from the Roll Back Malaria Partnership, to provide a standardized and cost-effective tool with which to evaluate the burden of malaria in an urban area in Africa. This methodology has been used to conduct assessments in Ouagadougou, Burkina Faso; Cotonou, Benin; Dar Es Salaam, Tanzania; and Abidjan, Ivory Coast.[3–7]

Health facility selection. We purposefully selected a sample of 30 government health facilities within Luanda. All government health facilities in Luanda province have been previously characterized by the Provincial Health Directorate (Direccão Provincial de Saúde, or DPS) as urban, peri-urban, or rural, based on vegetation, housing structure, water sources, and access to resources. Luanda province is divided into nine municípios (municipalities), within municípios into comunas (communes), and within comunas into bairros (neighborhoods), each of varying size and population density. Health facilities directed by the DPS include hospitals that have inpatient services, health centers staffed by doctors and offering a full range of services, and health posts, which offer fewer services and may not be staffed by a doctor. We attempted to select health facilities in each category proportional to the total number of facilities in each category. We also attempted, where possible, to select an equal number of health facilities in each of the urban, peri-urban, and rural strata, while also selecting a number of health facilities in each of the nine municípios of Luanda proportional to the number of health facilities in that município. City center was defined as the Ilha Health Center, as the margins of the city correspond approximately to a 15-km radius from that health center (Figure 1). As our objective was to examine the city of Luanda and immediate surrounding areas, health facilities more than 25 km from city center were excluded. There were 79 government health facilities in Luanda Province operating at the time of

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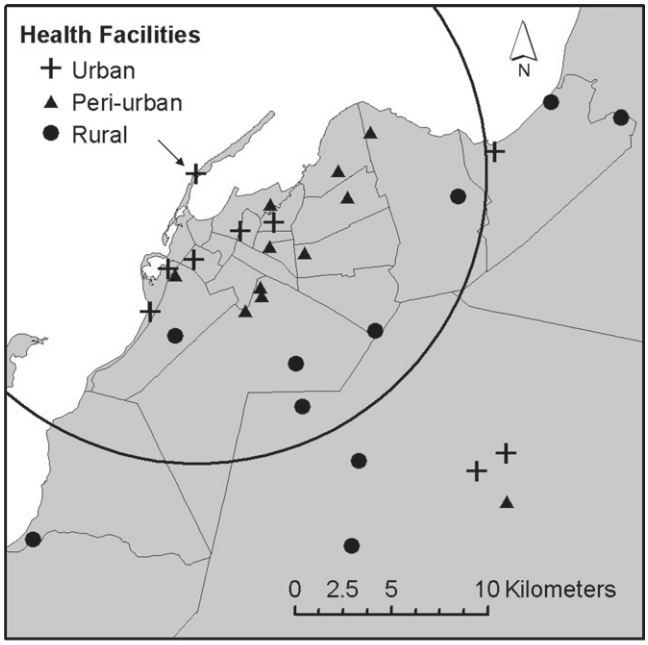


N.B. Some suburbs with areas classified as urban are developing on the outskirts of Luanda, accounting for a few urban health centers >15 km from city center.

FIGURE 1. Geographic distribution of health facilities (HF) selected, with 15 km radius centered on Ilha health center (denoted by arrow), approximating the boundaries of the city.

the assessment; 12 were > 25 km from city center and were excluded, leaving 67 health facilities from which the 30 were selected.

An assessment team consisting of nurse interviewers, an expert laboratory technician, and a supervisor visited each health facility for 1 day. Three teams visited 30 health facilities in 10 working days from March 17–31, 2008, which coincides with the rainy season and thus malaria transmission season.

Patient population. Adults and children presenting for their first outpatient consultation for the current illness with axillary temperature ≥ 37.5°C or history of fever in the past 24 hours, without signs of severe illness, weighing ≥ 5 kg, and not known to be in the first trimester of pregnancy (and thus unable to take Coartem) were eligible for enrollment. Nurse interviewers were assisted by health facility staff in patient recruitment. Patients were recruited sequentially after completing consultation with health facility staff. Up to 30 patients were recruited from each health facility on each day of study visit; if less than 30 febrile patients presented on that day, we enrolled the number of febrile patients who presented and consented. We obtained data regarding the total number of patients seen at each facility during the visit of the assessment team.

METHODS

For each patient, we performed an RDT (Paracheck, Orchid Diagnostics, Goa, India) and prepared thick and thin blood films to be stained and read later at the National Malaria Reference laboratory. Each patient also answered a questionnaire administered using personal digital assistants (PDAs) programmed in Visual CE (Syware, Cambridge, MA), regarding demographics, duration of fever, any prior treatment of this illness, use of bednets, housing type, water source, location of home, school, and job, and any travel in the previous 3 months. Any patient with a positive RDT was treated with artemether-lumefantrine, as per national policy in Angola.

Laboratory. All blood films were stained at the National Institute of Public Health Malaria Reference Laboratory in 10% Giemsa for 10 minutes, and read by two expert microscopists, with positivity, species, and density of asexual parasites and gametocytes recorded. Readers were blinded to RDT results and to each other's readings. Parasites and leukocytes were counted in the same fields until 200 leukocytes were counted. Parasite densities were estimated using an assumed leukocyte count of 8,000 leukocytes per μL of blood. Any slide for which there was disagreement in positivity or species, or discordance in density of greater than 50%, was read by a third expert microscopist, whose reading was considered final.

Data analysis. Data from the PDAs were downloaded daily for analysis. Questionnaire results were analyzed using SAS (version 9.1, SAS Institute, Cary, NC). A sample size of 900 is sufficient to estimate the proportion of febrile patients with laboratory-confirmed malaria within a precision of ±5% if the proportion ranges between 0.25 and 0.50 ($\alpha = 0.05$). This is also sufficient to estimate the proportion of patients with laboratory-confirmed malaria who had not traveled within a precision of ±5%, hypothesizing that the proportion is 0.95 ($\alpha = 0.05$). Univariate analysis was performed to determine significant associations with a positive blood film. We evaluated risk factors for a positive blood film in univariate analysis; variables with a P value of ≤ 0.15 were then evaluated in multivariate analysis. Clustering was accounted for in both univariate and multivariate analyses. A logistic regression model was constructed using backward elimination and adjusted odds ratios (AOR) were computed. Variables were retained in the final model if the associated P value for the AOR was < 0.05.

Ethical approval. The protocol received Human Subjects approval from Centers for Disease Control and Prevention, and concurrence from the Ministry of Health in Angola.

RESULTS

Patient characteristics. Of 2,348 total patients seen at the 30 health facilities on the day of visit, we enrolled 864 (36.8%). There were no refusals after recruitment by assessment staff. Of the 864 patients, 57.2% were female and 42.8% were male. Children < 5 years of age, children 5–14 years, and adults (≥ 15 years) made up 59.1%, 12.0%, and 28.9% of the assessment sample, respectively. Documented fever was noted in 47.7% of patients at the time of enrollment (median duration 3 days).

Of the total, 71.2% of patients were seen at health facilities < 15 km from city center, whereas 28.8% were seen at health facilities ≥ 15 km from the city center. Thirty-one percent of patients were seen at urban health facilities, 38.2% at peri-urban health facilities, and 30.8% at rural health facilities.

Only 10.2% of patients had been outside Luanda in the 3 previous months; 3.7% were visiting or had been residents for less than 3 months, and an additional 6.5% were permanent residents, but had traveled outside Luanda province in the previous 3 months. Proportions of patients who were residents and who had traveled outside Luanda were similar among urban, peri-urban, and rural health facilities.

Laboratory confirmed malaria. Of the 864 enrolled patients, 31 (3.6%) malaria blood films were positive. Blood films were positive in 2.4% of children < 5 years of age, 8.7% of

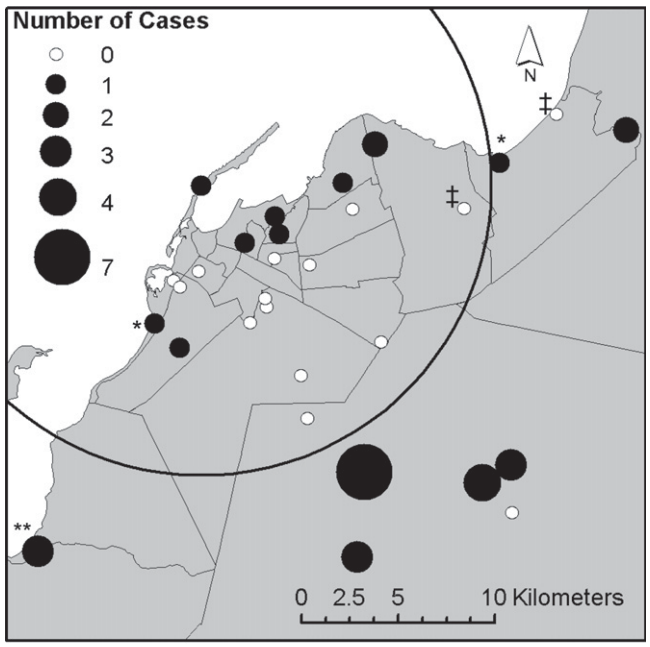
children 5–14 years, and 4.0% of adults. Children < 5 years of age were significantly less likely to have a positive blood film than older children and adults ($P = 0.03$). Among patients with documented fever at the time of enrollment, 4.6% had positive blood films, compared with 2.7% who were documented to be afebrile at the time of enrollment ($P = 0.11$).

Of note, 42 (4.9%) patients had a positive RDT and were treated with artemether-lumefantrine. There were 2 patients with a negative RDT who subsequently had a positive blood film; one had *Plasmodium malariae* (not detected by Paracheck). Compared with expert microscopy, RDTs in this setting had 96.7% (95% confidence interval [CI] 90.2–100.0%) sensitivity and 98.4% (95% CI 97.6–99.3%) specificity. Positive predictive value was 69.0%, but negative predictive value was 99.9%.

Urban, peri-urban, and rural health facilities and distance from city center. In health facilities classified as urban, 4.1% of patients had positive blood films, compared with 1.2% of patients in peri-urban health facilities, and 6.0% of patients in rural health facilities. The difference between peri-urban and rural film positivity rate was significant ($P = 0.006$). Using distance from city center, 1.5% of patients at health facilities < 15 km from city center had positive smears, compared with 8.8% of patients at health facilities ≥ 15 km from city center ($P < 0.0001$). Patients at health facilities ≥ 15 km from city center made up 28.8% of patients, but 71.0% of cases, and 21 of 28 patients with positive smears who were residents of Luanda lived in one of the three predominantly rural municípios: Cacuaco, Samba, and Viana (Figure 2). Because distance from city center was a far clearer risk factor for blood film positivity than urban, peri-urban, or rural health center classification, this determination was used for the remainder of the analyses.

Prior treatment. Just over half of the patients (54.6%) reported no prior treatment of this illness, whereas 40.7% reported treatment with acetaminophen only. Prior antimalarial use was reported by few patients for the current illness: chloroquine (0.5%), amodiaquine (0.9%), and artemisinins, either alone or in combination (3.2%). Ninety-nine (11.5%) patients reported being treated for malaria in the past 2 weeks; one had a positive blood film.

Insecticide-treated net use. Almost two-thirds (63.5%) of patients lived in households that owned ≥ 1 nets, whereas 55.1% lived in households that had hung ≥ 1 nets the previous night. Most nets (88.8%) in use by patients were reported to be long-lasting insecticide-treated nets (LLINs), and 34.1% had slept under an LLIN the night before. No non-LLIN was reported to have been treated with insecticide in the past 12 months. The proportion of patients who owned, hung, or slept under a net did not vary between health facilities < or ≥ 15 km from city center. For patients who owned a net, 3.1% had a positive blood film compared with 4.4% who did not own a net. For patients who hung a net, 2.5% had a positive blood film compared with 4.9% who did not hang a net. Finally, for patients who slept under an insecticide-treated net (ITN) the night before, 2.3% had a positive blood film compared with 4.3% who did not sleep under an ITN. None reached statistical significance in this sample (Table 1).



All but 5 health facilities enrolled 30 patients; exceptions are marked on the figure. ‡Enrolled 12 and 16 patients, no patients with positive films. *Enrolled 29 patients, 1 with a positive film. **Enrolled 28 patients, 3 with positive films.

FIGURE 2. Geographic distribution of malaria cases by health facility in Luanda, Angola.

TABLE 1
Univariate analysis of predictors of positive blood films among febrile patients in Luanda, Angola

Effect	Prevalence of variable	Prevalence of malaria in presence of variable	Odds ratio for blood film positivity	95% Confidence limits	*P* value
Documented fever at enrollment	412 (47.7%)	19 (4.6%)	1.77	0.88–3.59	0.11
Under 5 years	510 (59.0%)	12 (2.4%)	0.43	0.20–0.91	0.03
Male	369 (42.8%)	17 (4.6%)	1.66	0.86–3.19	0.13
Non-resident of Luanda	32 (3.7%)	3 (9.4%)	2.97	0.86–10.34	0.15
Outside Luanda in previous 3 months	88 (10.2%)	6 (6.8%)	2.20	0.68–13.07	0.13
HF ≥ 15 km from city center	249 (28.8%)	22 (8.8%)	6.53	2.90–14.68	< 0.0001
Work on a farm	39 (4.5%)	5 (12.8%)	4.52	1.48–13.77	0.008
5 minute walk to farm	155 (18.0%)	13 (8.4%)	3.51	1.31–9.46	0.01
5 minute walk to bus stop	165 (19.1%)	7 (3.4%)	1.25	0.59–2.62	0.56
5 min walk to open water source	296 (34.3%)	12 (4.1%)	1.22	0.72–2.08	0.46
Own net	549 (63.5%)	14 (3.1%)	0.69	0.30–1.57	0.37
Hung net the previous night	476 (55.1%)	12 (2.5%)	0.50	0.24–1.04	0.06
Under ITN the previous night	300 (34.7%)	7 (2.3%)	0.54	0.24–1.21	0.13

HF = health facility; ITN = insecticide-treated net.

TABLE 2

Multivariate model for predictors for positive blood film among febrile patients in Luanda, Angola

Effect	Odds ratio for blood film positivity	95% Confidence limits	*P* value
HF ≥ 15 km from city center	7.03	3.09–15.96	< 0.0001
Non-resident of Luanda	4.97	1.65–14.9	0.004
Documented fever	2.79	1.35–5.77	0.006
Under 5 years	0.31	0.12–0.81	0.02

HF = health facility.

Luanda residency status and travel. Of non-residents, 9.4% (3/32) had laboratory-confirmed malaria compared with 3.4% (28/832) of Luanda residents ($P = 0.15$), and 5.4% (3/56) of residents who traveled outside Luanda in the prior 3 months had laboratory-confirmed malaria compared with 3.4% (27/801) of those who had not ($P = 0.43$); neither was significantly different. When travelers and non-residents were grouped to compare all patients who had been outside Luanda in the previous 3 months to those who had not, there was a trend toward higher film positivity in the former group, but it was not significant (6.8% (6/88) versus 3.4% (25/776), $P = 0.13$) (Table 1).

Exposure history. Of the 4.5% of patients who reported working on a farm, 12.8% had positive blood films, compared with 3.2% that did not work on a farm ($P = 0.008$), and of the 18.0% who reporting living within a five minute walk of a farm, 8.4% of these had positive blood films compared with 2.5% of patients who did not ($P = 0.01$). Patients who reported living within a five minute walk of an open water source or interprovincial bus stop had similar rates of slide positivity as patients who did not (Table 1). Film positivity was not associated with educational attainment, studying or working at night, or housing or water type.

Multivariate analysis. In the final model, presenting to a health facility ≥ 15 km from city center, documented fever, and being a non-resident of Luanda were significantly associated with blood film positivity. Age < 5 years was negatively associated with blood film positivity (Table 2).

DISCUSSION

This assessment demonstrates that a very small minority of patients with fever at health facilities in Luanda city actually have laboratory-confirmed *Plasmodium* infection, despite the large proportion of patients being diagnosed and treated for malaria. These findings are consistent with population-based data from the 2006 Angola Malaria Indicator Survey showing the low prevalence of parasitemia among children < 5 years of age in Luanda province, as well as entomologic data showing that *Anophelines* make up a very small fraction of mosquitoes collected in Luanda. This low prevalence, even among those with fever, has two major implications: massive overuse of artemisinin-based combination therapies (ACTs) or other antimalarials in patients who do not need it, and likely underdiagnosis of other causes of fever, some of which may be potentially life-threatening. The higher incidence of malaria in older children and adults than in children < 5 years of age suggests delayed or non-existent acquisition of immunity. This further supports the hypothesis of a very low level of malaria transmission in Luanda; children < 5 years of age are more likely to be parasitemic than older age groups in areas of stable transmission.[8,9]

Travelers made up a small proportion of malaria cases; our data suggests that malaria imported from other parts of Angola does not make up a substantial proportion of malaria in Luanda province. Although non-residency was associated with blood film positivity in the final multivariate analysis, non-residents made up only 3.7% of the patient population. This is in contrast to other cities; in Antananarivo, Madagascar, the presence of antimalarial antibodies among residents was associated with travel outside the city.[10] Another study in Antananarivo found that only 1.9% of fevers were attributable to malaria, and that 80% of cases of malaria had traveled outside the city in the preceding 4 weeks.[11] In Luanda, the burden of malaria appears to be focused on the outskirts and in the surrounding rural areas of the province. At the time of the assessment, although RDTs and ACTs had been implemented in most health facilities in Luanda city, many health facilities further from city center did not yet have them. Our data suggest that resources for diagnosis and treatment of malaria, as well as resources for prevention, should be focused ≥ 15 km from city center.

There is also a pressing need for improved differential diagnosis of fever by health care workers and improved laboratory diagnosis for malaria in urban Luanda. Although our assessment did not directly assess laboratory diagnosis in health facilities, our data are in stark contrast to those from a database developed to track ACT use, in which > 50% of all blood films performed in Luanda are reported to be positive (Luvundo R, unpublished data). This discrepancy suggests that existing laboratory diagnosis is poor in Luanda. Corroborating evidence comes from a study completed nationwide under the auspices of the National Malaria Control Program, which found a 40% false positivity rate among blood films performed at the health facility level nationally (Fortes F, unpublished data). A further assessment to address causes of poor quality of laboratory diagnosis is needed, as are resources for diagnostic supplies and increased training and supervision. Although RDTs are available in most health facilities, and in trained hands perform well, there is anecdotal evidence of widespread distrust of negative results, and efforts to improve both laboratory performance of and provider confidence in RDTs are needed. Though the RDT positive predictive value of 69.0% seen in this assessment is not optimal compared with reference microscopy, a massive investment in retraining and supplies would be needed for health facility microscopists to surpass the accuracy of RDTs performed correctly.

Although this assessment is specific to Luanda, it brings up a number of important implications as Africa becomes more urbanized and as current malaria control efforts decrease malaria transmission. The phenomenon of lower prevalence of malaria in large urban settings is likely because of a confluence of factors, such as environments hostile to anopheline vectors, improvement in housing structures, altered vector and host behaviors, and improvement in access to prevention and treatment. In many places, health care providers continue to function in the "treat every fever as malaria" model. As the burden of malaria decreases, it unmasks the problem of other febrile illnesses, such as serious bacterial infections, which are more difficult to diagnose and treat. Mortality of children hospitalized for malaria was more than twice as high in children who had a clinical rather than laboratory diagnosis of malaria, suggesting that the excess mortality was a result of diseases other

than malaria.[12] Similar results were found among patients of all ages hospitalized for severe febrile illness in Tanzania.[13] Overdiagnosis and overtreatment of malaria are becoming increasingly problematic in the era of ACTs, because of greater expense and the concern of development of resistance.

This assessment had a number of limitations. Because it was health facility-based, it was not necessarily representative of the total population. Our assessment was limited to outpatient consultations of government health clinics, thus patients who accessed emergency rooms or private clinics were not included, and we do not have data regarding usage rates of public facilities. We were unable to ascertain the true denominator of febrile patients seen in the clinics, and used the total number of patients seen as a proxy; given that approximately half of patient visits are for fever and we enrolled over one-third, it is likely that we were able to enroll a majority of patients with fever or history of fever. Evaluation of care provided by the health facility was not a goal of this assessment; therefore, we did not collect information about what percent of enrolled patients were diagnosed with malaria and what treatment they received. We were also unable to collect complete geographic data on where the patient lived, worked, or had traveled within the city in the previous 3 months, though most presented to health facilities near where they lived and worked.

In summary, the low proportion of febrile patients in Luanda with laboratory-confirmed malaria is consistent with data from the 2006 Angola Malaria Indicator Survey and routine entomologic surveillance, and with results published from other large urban centers in Africa. This assessment provides much needed data with which to plan malaria control efforts in Luanda, and underscores the urgency in improving laboratory diagnostic capacity and rational antimalarial drug use.

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