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Factors associated with malaria case management practices at health facilities in Guinea during the 2014 Ebola outbreak

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An abstract of

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Abstract

Factors associated with malaria case management practices at health facilities in Guinea during the 2014 Ebola outbreak

Malaria is a critical public health problem in Guinea and is the primary cause of outpatient hospital visits. Malaria case management in the context of the Ebola Virus Disease (EVD) epidemic is complicated by similar clinical presentation of the two diseases, and malaria case management practices that require close patient contact and blood testing may place health workers at elevated risk of EVD infection. Information on malaria case management practices and determinants of those practices is needed to inform policy and training efforts aimed at reducing EVD transmission risk among health workers and reducing excess morbidity and mortality from incorrect malaria case management.

A retrospective register abstraction was performed at 120 health facilities in Guinea, and questionnaires were administered to health workers at each facility. Outcomes included malaria diagnostic testing for febrile patients, presumptive malaria treatment, and antimalarial treatment after diagnostic confirmation. Associations between each outcome and possible determinants were calculated using multivariate logistic regression models, controlling for expected confounders.

Among febrile patients, 61.9% received a malaria diagnostic test and 85.9% of patients with positive tests received antimalarial drugs, whereas 15.8% of all patients were presumptively treated without diagnostic confirmation. Report of EVD case(s) at health facilities was associated with lower odds of rapid diagnostic testing (aOR= 0.01, 95%CI: 0.001, 0.10) and higher odds of presumptive treatment (aOR= 30.7, 95%CI: 2.12, 444) compared to facilities that did not report EVD case(s). Complete PPE was only available at 6.2% of health facilities, and 21.8% of febrile patients received neither a malaria diagnostic test nor presumptive antimalarial treatment.

Malaria case management practices were highly associated with EVD case report at health facilities, and inadequate case management of febrile illness was common. As the EVD epidemic continues, training efforts may emphasize the importance of presumptive malaria treatment for reducing EVD transmission risk among health workers, especially at facilities that have not yet reported EVD cases(s). At facilities where adequate PPE is not available, presumptive malaria treatment should also be encouraged in order to reduce excess morbidity and mortality among febrile patients who do not receive malaria diagnostic tests.

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Thank you all,
Ian

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Acronyms

ACT: Artemisinin-based Combination Therapy

CDC: United States Centers for Disease Control and Prevention

CHW: Community Health Worker

CRS: Catholic Relief Services

DHS: Demographic and Health Survey

EVD: Ebola Virus Disease

GFATM: Global Fund for HIV/AIDS, TB and Malaria

LLIN: Long-lasting Insecticide Treated Net

MDA: Mass Drug Administration

PMI: President's Malaria Initiative

PPE: Personal Protective Equipment

RDT: Rapid Diagnostic Test

WHO: World Health Organization

Chapter 1: Background & Literature Review

Background

Malaria is a critical public health problem in Guinea, where 100% of the population is at risk (1, 2). Proper case management is an essential strategy for control (3), but has become extremely complicated in the context of the 2014-2015 Ebola virus disease (EVD) epidemic (4). This study explored factors associated with malaria case management practices in the context of the EVD epidemic with the goal of supporting efforts to mitigate nosocomial EVD infection and secondary public health consequences due to inadequate or incorrect management of malaria patients at Guinean health facilities. Below is a review of the literature that informed this study, including malaria epidemiology and control efforts in Guinea, the 2014-2015 EVD outbreak in Guinea and its effects on the health system, the intersection of EVD and malaria in Guinea, and factors associated with malaria case management practices among health workers.

Literature Review

Malaria in Guinea

Malaria is one of the most important public health problems in Guinea. 100% of the population is at risk for the disease, and the risk is much higher for children under five years old and pregnant women (2). Malaria parasitemia prevalence among children under five as measured by microscopy varies by region from 3% to 66% with a national average of 44% (5). Malaria accounts for 31% of hospital consultations, 25% of hospitalizations, and 14% of hospital deaths (1)[1].

[1] All malaria statistics were measured prior to the EVD outbreak, unless otherwise specified

The National Malaria Control Program (NMCP) is responsible for malaria control efforts in Guinea, and receives support from the President's Malaria Initiative (PMI), the Global Fund for HIV/AIDS, TB and Malaria (GFATM), and other donors and partners. Principal malaria control activities include distribution of long lasting insecticide treated nets (LLINS), the scale-up of appropriate malaria case management, and the treatment and prevention of malaria in pregnancy. The main objective of malaria control efforts in Guinea is to reduce malaria morbidity and mortality by 50% by 2015 (2).

Appropriate malaria case management includes early diagnosis and rapid treatment with effective antimalarial drugs (6). Suspect malaria cases in Guinea should be confirmed by microscopy or rapid diagnostic test (RDT). The first-line treatment is an artemisinin combination therapy (ACT), artesunate amodiaquine (AS-AQ), for uncomplicated cases, and injectable artesunate for severe cases (2). Appropriate malaria case management is essential for reducing individual-level malaria morbidity and mortality as well as achieving population-level malaria control goals (7, 8).

Data from the 2012 DHS show relatively low rates of healthcare attendance and treatment for malaria cases. In the two weeks prior to the survey, less than 40% of children under five sought advice or treatment for fever, and only 28% were prescribed an antimalarial treatment. Although early diagnosis and treatment is an essential for effective case management, only 1% of febrile children received a first-line antimalarial drug on the same or next day after fever onset (5).

Malaria management in Guinea is implemented through a multi-tiered health system. At the lowest level of the health system, community health workers (CHWs) provide testing and treatment for uncomplicated malaria cases. Public health facilities are organized geographically and by size and specialization of treatment offered. There are 963 health posts in Guinea, which are staffed by trained clinical officers and serve small populations

of around 3,000 people. The next health facility level consists of 413 health centers, which provide health care and supervise health posts. CHWs are typically attached to and supervised by health centers as well. Finally, each of the 33 districts in Guinea has a district hospital which serves as a reference center and serves an average of 285,000 people (2).

The 2014-2015 EVD epidemic in Guinea

The 2014-2015 epidemic in West Africa is the largest EVD outbreak ever recorded (9). As of March 18th, 2015 there have been over 25,000 reported confirmed, probable, and suspected cases of the disease in Guinea, Liberia, and Sierra Leone. Although the outcome for many cases remains unknown, there have been at least 10,000 reported deaths. Guinea alone has reported 3,389 EVD cases with 2,224 reported deaths, representing a 66% mortality rate (10)[2].

On March 10, 2014, public health services in two prefectures in the forested region of Guinea notified the ministry of health about clusters of an unidentified, deadly disease characterized by fever, vomiting, diarrhea, and a high fatality rate. Subsequent epidemiological investigations later identified a two year old child who died in the prefecture of Guéckédou on December 6, 2013 as the probable first case (11). Although the disease source is not certain, fruit bats have been frequently identified as a possible reservoir. Three species of fruit bats are common throughout many parts of West Africa (12), which suggests that EVD could have existed in the region prior to its detection. By the end of March, EVD cases began to be reported in parts of Liberia that border the initially affected prefectures in Guinea, and the first cases in Sierra Leone were reported

[2] See http://apps.who.int/ebola/current-situation/ebola-situation-report-1-april-2015-0 for a map of the epidemic in Guinea and surrounding countries.

in May. In August 2014, the World Health Organization (WHO) declared the epidemic an international public health emergency (13).

As in previous outbreaks in central Africa, poor public health infrastructure and the relative remoteness of the regions where the virus first occurred probably served to propagate the outbreak. Lack of infection control procedures and inadequate resources predictably proved major challenges to infection control, treatment, and contact tracing efforts (14, 15). The epidemiology of the 2014 epidemic diverged importantly from any prior EVD outbreak when urban transmission, primarily in Liberia's capital, began to accelerate exponentially (16).

Nosocomial transmission and transmission to healthcare workers are particular sources of concern during the ongoing EVD epidemic (17). As of March 18th, 2015, more than 850 health care workers had been infected and 492 had died (10). A report from Sierra Leone found that healthcare workers were at nearly a 100 times greater risk of EVD infection than the general population. Risk factors for health worker transmission included lack of infection control procedures, inadequate personal protective equipment, and non-distinction between low and high risk areas in Ebola treatment units (ETUs) (18). Though nosocomial transmission is frequently described in the case of health workers caring for confirmed EVD patients, care for unconfirmed but symptomatic cases is another likely driver of health worker infection (16).

Although transmission in Guinea has slowed significantly in 2015 from its peak in the fall of 2014, important challenges remain before the epidemic is completely controlled and transmission halted. Unsafe burials and limited early detection of cases are two significant challenges to complete transmission reduction. Almost half (23) of all the EVD cases registered in the week of March 15th, 2015, for example, were registered post-mortem (10).

EVD and malaria case management in Guinea

In addition to its direct effects, the 2014-2015 EVD epidemic has likely had enormous indirect effects on the health systems and populations in Guinea, Liberia, and Sierra Leone. A small and compromised workforce and widespread closures of health facilities have had devastating effects on general health care in the affected countries (19). Childhood vaccination campaigns have been delayed or halted, leading some to predict potentially devastating outbreaks of measles and other vaccine-preventable diseases in the coming months (20). Widespread fear and misinformation have also likely resulted in a significant decrease in health facility attendance in Guinea. As much as 74,000 fewer malaria cases may have presented at Guinean health facilities in 2014 because of Ebola-related fears, resulting in an estimated 7,600 excess deaths due to malaria (21).

Appropriate diagnosis and case management of malaria and EVD are particularly challenging for healthcare workers in Ebola-affected countries. The initial presentation of both diseases is almost identical, and includes fever, chills, and malaise (4). Laboratory confirmation is required in order to correctly diagnosis EVD (22), and microscopy or rapid diagnostic tests (RDTs) are used for malaria diagnosis (3). During the EVD Epidemic in Conakry, Guinea's capital city, up to 70% of EVD patients had simultaneous malaria infections (23), further complicating diagnosis and management of these two illnesses.

Challenges in differentiating, diagnosing, and treating malaria and EVD have the potential to both magnify Ebola transmission as well as increase malaria morbidity and mortality in Guinea and other affected countries. If, for example, a healthcare worker performs a malaria diagnostic test or microscopy for a suspected malaria patient but the patient actually has EVD, the risk for EVD infection for the provider may be high in the absence of adequate personal protective equipment (PPE). If a malaria patient is either sent to an Ebola treatment center or not treated at all, his or her risk for further complications from

malaria and potential for contracting EVD at the treatment center may both be elevated. These problems, in the absence of adequate PPE, infection control procedures, and isolation wards, have contributed to high rates of health worker infection and to hospitals becoming amplification points for EVD transmission in the most affected countries (24). Caring for symptomatic but unconfirmed EVD patients is likely a significant cause of health worker EVD infection (16).

In November 2014, the World Health Organization issued temporary guidelines for the management of malaria cases in Ebola-affected countries. The guidelines state that adequate (PPE) must be used for the administration of (RDTs) to suspect malaria cases. Adequate PPE includes double examination gloves, face shield, and disposable gown for patients without vomiting, bleeding, or diarrhea. Head covers, boots, and impermeable gowns are also required for patients with vomiting, bleeding, or diarrhea. In the absence of adequate PPE, WHO recommends suspension of RDT use and presumptive treatment of all suspected malaria cases with first-line antimalarial drugs. These guidelines were designed to reduce malaria morbidity and mortality in affected countries, reduce malaria-related strain on the health system in order to redirect resources to Ebola response, and increase health worker protection (4).

Mass drug administration (MDA) is another tool that has been piloted to mitigate the impact of the Ebola epidemic on malaria morbidity and mortality in Guinea, Liberia, and Sierra Leone. In MDA campaigns health workers distribute first-line antimalarial drugs to all eligible people in targeted areas, regardless of symptoms. These campaigns have reached more than 3 million people since 2014 and are presumed to have reduced malaria prevalence in the population and to have reduced risk of nosocomial EVD transmission to malaria patients at health facilities (25).

Factors associated with malaria case management practices

As has been previously described, nosocomial transmission and transmission to front-line health workers is of special concern during EVD outbreaks (16, 26). Nosocomial transmission is an important amplification point for EVD outbreaks (27). Incorrect case management of febrile patients during EVD outbreaks may not only be a driving factor of health facility-based Ebola transmission (16), but also of increased patient morbidity and mortality from other diseases such as malaria (4).

Although factors related to health worker case management in the context of Ebola have been studied (18), there is little information available about malaria case management practices among health workers in the context of EVD outbreaks. There is also a dearth of information about the main drivers of these practices, despite the recognition that malaria case management practices among health workers could serve to either limit or amplify the risk of EVD transmission in healthcare settings (4).

There have been a few studies in sub-Saharan Africa that assessed the factors associated with appropriate malaria case management practice among health workers. In Tanzania, more than three years of experience and job position (clinical officer or lower cadre versus medical officer) were positively associated with likelihood to correctly prescribe ACTs to malarial patients. Conversely, supervisory visits, training on ACT use, and the availability of job aids did not significantly predict correct ACT prescription (28). In Cameroon, a three-day refresher training was positively associated with higher likelihood of appropriate RDT use among health workers compared to a basic one-day refresher training or no extra training. However, neither one-day nor three-day refresher trainings significantly impacted appropriate ACT prescription (29). Patient demands, drug shortages, financial influences, and prescribing attitudes all contribute to insufficient adherence to case management guidelines among healthcare workers (30-32). In Malawi,

only patient-level predictors such as spontaneous complaint of fever and health worker position were associated with case management quality. Other health worker-, health facility-, and regional-level factors were not associated with case management practice (33).

Chapter II: Manuscript

Title

Factors associated with malaria case management practices at health facilities in Guinea during the 2014 Ebola outbreak

Abstract

Malaria is a critical public health problem in Guinea and is the primary cause of outpatient hospital visits. Malaria case management in the context of the Ebola Virus Disease (EVD) epidemic is complicated by similar clinical presentation of the two diseases, and malaria case management practices that require close patient contact and blood testing may place health workers at elevated risk of EVD infection. Information on malaria case management practices and determinants of those practices is needed to inform policy and training efforts aimed at reducing EVD transmission risk among health workers and reducing excess morbidity and mortality from incorrect malaria case management.

A retrospective register abstraction was performed at 120 health facilities in Guinea, and questionnaires were administered to health workers at each facility. Outcomes included malaria diagnostic testing for febrile patients, presumptive malaria treatment, and antimalarial treatment after diagnostic confirmation. Associations between each outcome and possible determinants were calculated using multivariate logistic regression models, controlling for expected confounders.

Among febrile patients, 61.9% received a malaria diagnostic test and 85.9% of patients with positive tests received antimalarial drugs, whereas 15.8% of all patients were presumptively treated without diagnostic confirmation. Report of EVD case(s) at health facilities was associated with lower odds of rapid diagnostic testing (aOR= 0.01, 95%CI: 0.001, 0.10) and higher odds of presumptive treatment (aOR= 30.7, 95%CI: 2.12, 444) compared to facilities that did not report EVD case(s). Complete PPE was only available at 6.2% of health facilities, and 21.8% of febrile patients received neither a malaria diagnostic test nor presumptive antimalarial treatment.

Malaria case management practices were highly associated with EVD case report at health facilities, and inadequate case management of febrile illness was common. As the EVD epidemic continues, training efforts may emphasize the importance of presumptive malaria treatment for reducing EVD transmission risk among health workers, especially at facilities that have not yet reported EVD cases(s). At facilities where adequate PPE is not available, presumptive malaria treatment should also be encouraged in order to reduce excess morbidity and mortality among febrile patients who do not receive malaria diagnostic tests.

Introduction

As of writing on March 18th, 2015, the World Health Organization (10) has reported more than 25,000 Ebola Virus Disease (EVD) cases and 10,000 EVD-related deaths, the overwhelming majority of which have occurred in Guinea, Liberia, and Sierra Leone. Though the virus has declined in Liberia, transmission remains high in Sierra Leone and continues with no discernible downward trend in Guinea. Guinea has registered 3,398 confirmed, probable, and suspected cases, with 95 in the week prior to March 18th, 2015. This was the highest weekly total in 2015. To date there have been more than 2,224 Ebola related deaths in Guinea (10).

Beyond its immense effect on those infected with EVD, the outbreak has had considerable secondary public health consequences in Guinea and the other affected countries, especially in relation to malaria control and case management. Malaria is a critical public health problem in Guinea, accounting for 31% of hospital consultations, 25% of hospitalizations, and 14% of hospital deaths (1). There have been reports that the outbreak has virtually shut down malaria control efforts, including distributions of long-lasting insecticide treated nets (LLINs) and indoor residual spraying (IRS) campaigns (34). With 100% of the population of Guinea at risk for malaria (2), the halting of major control programs could significantly increase malaria transmission.

The outbreak has also impacted malaria treatment seeking and case management. Numerous health structures have been closed, and in the facilities that remain open, outpatient malaria visits have dropped by as much as 90%. Widespread fear of contracting EVD or of being diagnosed with EVD has prevented many malaria patients from seeking care (4). It is likely that these factors have contributed to an acute increase in malaria morbidity and mortality in Ebola affected countries. Some sources have estimated that

malaria deaths quadrupled in 2014 (35), and a recent study estimated that up to 74,000 malaria cases did not seek care at health facilities in 2014 due to Ebola related fears. This dramatic drop in treatment seeking resulted in an estimated 7,600 excess deaths from malaria in 2014 (21).

Appropriate diagnosis and case management of malaria and EVD is particularly challenging for health workers in Ebola-affected countries. The initial presentation of both diseases is almost identical, and includes fever, chills, and malaise (4). Laboratory confirmation is required in order to correctly diagnosis EVD (22), and microscopy or rapid diagnostic tests (RDTs) are used to diagnose malaria (3). Up to 70% of EVD patients had simultaneous malaria infections in Guinea (23), further complicating diagnosis and management of the two illnesses.

Ebola transmission and malaria morbidity may both be amplified by the challenges in differentiating and diagnosing the two diseases at the health facility level. If, for example, a healthcare worker performs a malaria diagnostic test or microscopy for a suspected malaria patient but the patient actually has EVD, the risk for EVD infection for the provider is likely high in the absence of adequate personal protective equipment (PPE). If a malaria patient is either sent to an Ebola treatment center or not treated at all, his or her potential for contracting EVD at the treatment center and risk for further complications from malaria are likely both elevated. These problems, in the absence of adequate PPE, infection control procedures, and isolation wards, have contributed to high rates of health worker infection and to hospitals becoming amplification points for EVD transmission in the most affected countries (24). In Sierra Leone, EVD incidence was approximately 100 times higher in health care workers compared to the rest of the population, likely due to inadequate PPE and infection control procedures at health facilities (18).

Little is known about the case management practices of Guinean health workers during the Ebola epidemic. Although guidelines and trainings on the case management of Ebola were variously disseminated throughout the EVD epidemic in 2014, these guidelines were never standardized at the national level and there was likely significant variation in their reach and the extent to which they were observed by health workers (36). In November 2014, the WHO issued temporary guidelines for the management of suspect malaria cases in Ebola affected countries. According to those guidelines, malaria RDTs should only be performed in the presence of adequate PPE, including double examination gloves, face shield, and disposable gown for patients without vomiting, bleeding, or diarrhea and with the addition of head covers, boots, and impermeable gowns for patients with any of those symptoms. In the absence of adequate PPE, ACTs should be prescribed presumptively for any suspect malaria patient (4).

National guidelines for malaria case management in the context of the EVD-epidemic were not standardized and disseminated in Guinea until February, 2015 (36). Malaria case management, including diagnostic testing and antimalarial prescription, thus remained relatively unregulated during the 2014 EVD epidemic. Little information was available to policy makers about what case management practice continued to be undertaken at the health facility level, or what factors influenced those practices.

Information is somewhat limited about factors associated with malaria case management practices among health workers in sub-Saharan Africa. In Tanzania, more than three years of experience and job position (clinical officer or lower cadre versus medical officer) were positively associated with likelihood to correctly prescribe ACTs to malarial patients. Conversely, supervisory visits, training on ACT use, and the availability of job aids did not significantly predict correct ACT prescription (28). In Cameroon, a three-day training was positively associated with appropriate RDT use compared to a basic one-day training or

no extra training. However, neither one-day nor three-day trainings significantly impacted appropriate ACT prescription (29). Patient demands, drug shortages, financial influences, and prescribing attitudes all contribute to insufficient adherence to case management guidelines among healthcare workers (30-32). In Malawi, only patient-level predictors such as spontaneous complaint of fever and health worker position were associated with case management quality. Other health worker-, health facility-, and regional-level factors were not associated with case management practice (33).

Appropriate malaria case management may reduce malaria morbidity and mortality in Guinea, regardless of the EVD outbreak. In neighboring Guinea Bissau, for example, strict adherence among healthcare workers to malaria case management guidelines was associated with a 50% reduction in in-hospital malaria mortality and a 40% reduction in cumulative 4-week mortality (37). In the context of the ongoing EVD epidemic, improved case management of febrile illness will also protect front-line healthcare workers and increase the health system's capacity to respond to EVD cases (4, 24). Identifying the primary factors that influence malaria case management practices among healthcare workers will help the NMCP target policy and information dissemination efforts aimed at limiting EVD transmission risk in healthcare settings and mitigating excess malaria morbidity and mortality.

This analysis explored the main factors associated with malaria case management practice at health facilities in Guinea, with the aim of supporting the NMCPs policy and information dissemination efforts in the context of the ongoing Ebola outbreak in Guinea. Case management practices of primary interest were malaria diagnostic testing for febrile patients and antimalarial prescription, including presumptive treatment and treatment for positive diagnostic tests. The main research objectives were to describe these case management practices at health facilities in November 2014 in EVD-affected compared to

unaffected districts, and secondly identify district-, facility-, and patient-level factors associated with these practices.

Methods:

Data Source:

This study was a secondary analysis of data from a program evaluation conducted in December 2014 by the NMCP of Guinea with support from Catholic Relief Services (CRS), GFATM, the US Centers for Disease Control and Prevention (CDC), and the President's Malaria Initiative (PMI). The evaluation consisted of two components: a retrospective review of health facility registers, as well as quantitative health worker interviews.

Study Site and Sampling:

Our evaluation utilized a cross-sectional design, where we compared malaria case diagnosis and treatment (dependent variables) between districts most affected or unaffected (primary exposure variable) by the EVD epidemic. Of the 22 EVD-affected districts as of November 1st, 2014, four were randomly selected through random number generation. These included the districts of Guéckédou, Kerouane, Macenta, and Conakry. The first three districts are in the forested region in southeastern Guinea, while Conakry is the capital on the east coast of the country and is home to almost 2 million people (38). Four out of the 10 unaffected districts at the time of the study were selected and included Fria, Gaoual, Labe, and Mandiana. The unaffected districts were located mostly in the north and northwest of the country. Study locations are presented in **Figure 1.**

In each of the eight study districts, we selected 15 health facilities: seven health centers and seven health posts were randomly sampled from a list of all health centers and health posts in each district, and the main district hospital in each district was automatically included. A total of 120 health facilities were selected in the sample, 60 of which were in Ebola-affected districts and 60 of which were in non-affected districts. Sample size was based on logistic and budgetary considerations.

Data Collection:

Retrospective register abstractions were conducted by trained survey teams at each facility and consisted of two parts. In health centers and health posts, 40 patient entries were randomly sampled for the months of November 2014 and November 2013 in order to provide a representative sample of case management practices at each particular facility during each particular month. November is typically the end of the high malaria transmission period which lasts from May to December (5). In hospitals with multiple wards, pediatric and general wards were treated as individual sampling units and 40 patient entries were sampled from each ward register. Only 40 patient entries were sampled from registers in hospitals without multiple wards. **Figure 2** details this data collection and sampling scheme. Information collected included a patient's age, history of fever, malaria diagnostic testing, and antimalarial prescription (see Appendix 1). The second phase of register abstraction consisted of an aggregate abstraction of patient data for January through November 2013 (prior to the outbreak) and 2014. Data collected during this phase was aggregated by month and included total patients seen, total febrile patients, total diagnostic tests performed, and total antimalarial treatments administered (Appendix II).

Questionnaires on malaria and Ebola case management practices were administered to one person in charge of each health post and health center, typically the head nurse or doctor. At the larger district hospitals, three clinicians were asked to respond to the questionnaire, typically the head doctor and two nurses. Survey questions addressed malaria case management practices before and after the beginning of the epidemic, procedures for handling suspect Ebola cases, training and supervision, reported availability of personal protective equipment and malaria diagnostic tests and drugs, and patients' attitudes towards health care services since the beginning of the epidemic (see Appendix III). Surveyors obtained verbal consent from all health workers prior to administration of the questionnaire (Appendix IV).

Outcome and Variable Definitions

The primary outcomes were malaria diagnostic testing for febrile cases (i.e., diagnostic testing) and antimalarial prescription, including presumptive prescription of antimalarial drugs without prior diagnostic confirmation (i.e., presumptive treatment) and antimalarial prescription for patients with positive diagnostic confirmation (i.e., positive treatment). Diagnostic testing for febrile cases was defined as a record of malaria RDT or microscopy testing for any patient who presented with history of fever at the health facility. Antimalarial prescription included the recorded prescription of any type of antimalarial drug, including ACTs, injectable quinine, or any other unspecified type of antimalarial drug. Presumptive treatment was defined as the prescription of any type of antimalarial drug to a patient without prior diagnostic confirmation by malaria RDT or microscopy. Positive treatment was defined as prescription of any antimalarial drug for a patient following a positive malaria diagnostic test.

Exploratory analysis examined possible district-, facility-, and patient-level determinants of diagnostic testing, presumptive treatment, and positive treatment. At the district level, location in an EVD-affected district compared to location in an unaffected district was considered. At the facility level, associations of interest included report of cases(s) of EVD seen at the health facility (i.e., EVD case report), reported health worker participation in malaria trainings in the context of the EVD epidemic, EVD trainings, and PPE trainings, availability of examination gloves and availability of complete PPE. Availability of examination gloves was defined as the availability of greater than or equal to 100% of monthly glove consumption average at facility at time of survey. With the exception of complete PPE, this definition format was used as a proxy for the availability of all commodities at the time of patient visit because commodity data are not typically recorded on patient registries. Complete PPE availability was defined as health worker reported availability of face shield, helmet, impermeable gown, and boots in addition to examination gloves at time of survey, but data on stocks and monthly consumption averages were not provided for these items. Fever and age category, dichotomously defined as < 5 years old or ≥ 5 years old, were patient-level factors included as a possible determinant of malaria case management practice.

Expected confounders were simultaneously controlled for in the analysis. For the outcome of diagnostic testing for febrile patients, confounders included facility type, availability of RDTs (defined as ≥100% of monthly RDT consumption average available at time of survey), and diagnostic testing for febrile patients at each facility during November 2013. For the outcome of presumptive treatment and positive treatment with antimalarial drugs, confounders included facility type, availability of antimalarial drugs (defined as ≥100% of monthly antimalarial drug consumption average available at time of survey), and presumptive treatment or positive treatment for patients at each facility during November 2013.

Analysis

Analysis was performed using R survey software and Statistical Analysis Software (SAS) version 9.4 and consisted of two steps. First, unweighted statistics were calculated on the characteristics of facilities included in the sample, stratified by Ebola-affected districts versus non-affected districts. Characteristics included facility types, malaria RDT availability, antimalarial drug availability, glove availability, complete PPE availability, health workers' reported participation in malaria case management trainings in the context of the Ebola epidemic, Ebola-specific trainings, and PPE trainings, and facilities reporting having received a case of Ebola at their facility. Bivariate logistic regression models using SAS proc surveylogistic were used to measure differences in each of these characteristics between Ebola-affected versus unaffected districts, adjusting for clustering at the health facility level.

Second, associations were calculated between possible determinants and three outcomes of interest: 1) diagnostic testing, 2) presumptive treatment, and 3) positive treatment. Sampling weights were applied and represented the inverse of the probability of selection for each facility times the probability of selection of each patient entry. Because there was only one hospital in each district, a strata statement was applied in which each district hospital was assigned its own stratum level. Health posts and health centers were assigned group strata levels. Unadjusted logistic regression models produced unadjusted estimates of the effect of each independent variable on each primary outcome. Multivariable analysis was then used to assess independent relationships between all measured determinants and malaria case management outcomes, controlling for expected confounders. Unadjusted odds ratios (OR) and adjusted odds ratios (aOR) were reported for each independent variable of interest, along with accompanying 95% Confidence Intervals (95% CI) and 2-sided *P* - values where values less than or equal to $\alpha = 0.05$ were considered

significant. All measures of association incorporated survey weights and strata, adjusting for clustering at the health facility level; model fit was assessed using Goodness of Fit tests.

Ethics:

This study included secondary analysis of de-identified data obtained by the NMCP of Guinea during a program evaluation; the study was deemed exempt by Emory University's Institutional Review Board.

Results

Characteristics of surveyed facilities

Five (6%) of the 60 sampled health facilities in EVD affected districts were closed due to the EVD epidemic and were therefore not included in the register abstractions or health worker questionnaires. Two (3%) of the 60 facilities in unaffected districts were also permanently closed and not included. Health workers questionnaires and register abstractions were performed at all open facilities. **Table 1** shows the characteristics of the 113 operational facilities at which data was collected, stratified by EVD-affected zone compared to unaffected zone. Monthly supplies of malaria commodities including RDTs and antimalarial drugs were widely available in >70% of facilities, and did not significantly differ between zones. Reported health worker participation in malaria trainings, EVD trainings, and PPE trainings were all significantly higher in EVD-affected zones.

At the time of the data collection and survey period on December 31st, 2014, there had been no reports of confirmed EVD cases in any of the unaffected districts included in our sample (39). Health workers in both EVD-affected and unaffected districts nevertheless reported having seen suspect or confirmed EVD case(s) at their facility. Among facilities in EVD-

affected districts, 17 (30.9%) reported having received at least one EVD case at their facility, whereas 5 (8.6%) of facilities in EVD-unaffected districts also reported actually having seen at least one case of EVD at their facility. These reports reflected health worker perceptions and were not verified using patient records.

Malaria case management characteristics at surveyed health facilities

Table 2 shows weighted patient demographics and malaria case management characteristics at health facilities in November 2014, stratified by Ebola affected and unaffected zones. Significantly more patients in unaffected zones were ≥5 years old (P = 0.007), whereas the percent of patients who presented with fever did not differ significantly between zones and averaged 61.9%. Malaria diagnostic testing was moderate and not significantly different across zones (P = 0.26), with an overall average of 58.8% of all febrile patients receiving a diagnostic test.

Of all patients visiting health facilities, 43.5% received some type of antimalarial drug. Antimalarial prescription for diagnostically confirmed cases did not differ across zones (P = 0.09), and averaged 85.9%. Of all patients visiting health facilities, 15.7% were treated presumptively for malaria without diagnostic confirmation. This did not differ by zone (P = 0.42).

Malaria case management practices for febrile patients are represented in **Figure 3**. WHO 2014 guidelines for the management of suspect malaria cases during the EVD epidemic recommend malaria diagnostic testing of suspect malaria patients only if adequate PPE is available, else febrile patients should be presumptively treated with first-line antimalarial

drugs (4)[3]. Using these guidelines, an estimated 68.5% of febrile patients received appropriate malaria case management through antimalarial prescription after a positive test, presumptive antimalarial prescription without diagnostic testing, or no antimalarial prescription after a negative diagnostic test. The remaining 31.5% of febrile patients did not receive correct malaria case management. Incorrect malaria case management included antimalarial prescription despite a negative diagnostic test (4.1%), no antimalarial prescription despite a positive test (5.6%), and no presumptive treatment when no diagnostic test was performed (21.8%).

Rainfall and other environmental drivers of malaria transmission did not significantly change from 2013 to 2014, so it is unlikely that malaria transmission ecology and epidemiology changed from one year to the next (21). Nevertheless, Guinean health facilities saw an important decline in malaria case-load in 2014 compared to 2014. **Figure 4** depicts seasonal malaria trends in Guinea as well as an important drop in malaria case-load at surveyed health facilities during 2014 compared to 2013. Average malaria cases per facility dropped from 164.8 in November 2013 to 115.9 in the same month in 2014. This decline is likely attributable to decreased malaria treatment seeking behavior due to EVD-related fears.

Factors associated with diagnostic testing for febrile patients

[3] Although data were not availability on the point-availability of PPE for each patient seen, we may conclude that, at a minimum, febrile patients should have either received a diagnostic test or have been presumptively treated with antimalarial drugs in the absence of a test. Patients with positive diagnostic tests should receive antimalarial drugs, whereas negative tests should not be treated with antimalarial drugs. Data were not available to assess the appropriateness of the type of antimalarial drug prescribed because information was not collected on disease severity or actual drug for all antimalarial drugs classified as “other”.

Overall, 1,786 patients (35.0%) at sampled health facilities in November 2014 received a malaria diagnostic test. The majority of malaria tests performed were RDTs (89.0%), whereas 9.0% of tests were by microscopy and 2.0% of tested patients received both microscopy and an RDT. The majority of tests performed were for febrile patients (88.6%), although only 64.2% of all febrile patients actually received a malaria diagnostic test.

Table 3 presents district-level, facility-level, and patient-level factors associated with malaria diagnostic testing for febrile patients, as well as expected confounders. At the district level, location in an EVD-affected zone was not associated with any significant change in diagnostic testing for febrile patients ($P = 0.29$).

Adjusting for other factors, facility-level factors were most strongly associated with diagnostic testing of febrile patients. EVD case report was associated with a dramatically lower odds of diagnostic testing of febrile patients (aOR= 0.01, 95%CI: 0.001, 0.10). Reported participation in PPE trainings was conversely associated with a five-times higher likelihood of diagnostic testing for febrile patients (aOR= 5.62, 95%CI: 1.88, 16.8). At the patient level, age did not appear to be associated with any change in diagnostic testing for febrile patients ($P = 0.17$).

Factors associated with presumptive antimalarial drug prescription

A total of 523 (15.7%) patients were presumptively treated with antimalarial drugs without prior diagnostic confirmation in November 2014. Among presumptively treated patients, the majority (64.8%) of patients were prescribed only ACTs. 50 patients (9.6%) received only injectable quinine, 122 (23.3%) patients received an unspecified type of antimalarial drug, and the rest received some combination of ACTs, quinine, and other antimalarial drugs.

Table 4 shows associations between district-, facility-, and patient-level factors and presumptive treatment, including measured confounders. At the district level, location in an EVD-affected zone was not associated with any change in the likelihood of presumptive treatment for febrile patients (P = 0.22).

At the facility level, EVD case report and glove availability were inversely associated with presumptive treatment when adjusting for all other factors. EVD case report was associated with a 30 times higher odds of presumptive treatment (aOR= 30.7, 95%CI: 2.12, 444), whereas a month-supply of gloves was associated with an 87.3% lower odds of presumptive treatment (aOR= 0.13, 95%CI: 0.04, 0.41). At the patient level, fever was associated with higher odds of presumptive treatment (aOR= 2.28, 95%CI: 1.17, 4.46).

Factors associated with treatment with antimalarial drugs after prior diagnostic confirmation

Of the 1,767 patients in the sample who received a malaria diagnostic test, 1,345 (76.1%) were positive. Most diagnostically confirmed cases (85.9%) received some sort of antimalarial. Of the antimalarial drugs prescribed to patients with positive diagnostic tests, ACTs were most common, followed by quinine and other antimalarial drugs.

Table 5 shows factors associated with positive treatment with antimalarial drugs after prior diagnostic confirmation. Prior to adjusting for any other covariates, health workers' reported participation in Malaria, EVD, and PPE trainings, availability of complete PPE, and fever all appear to be associated with higher odds of positive treatment. However, when adjusting for all other factors, only fever and availability of complete PPE were independently associated with likelihood of antimalarial prescription for diagnostically confirmed malaria patients in November 2014. Full PPE availability was associated with a

29-fold higher odds of positive treatment (aOR 29.1, 95%CI: 1.23, 688), and fever was associated with an 8-fold higher odds of positive treatment (aOR 8.30, 95%CI: 3.20, 21.5).

Discussion

Here we describe trends in malaria case management practice at health facilities during the 2014 EVD epidemic in Guinea and investigate district-, facility-, and patient-level factors that were associated with these practices. Our results reveal the important influence of EVD case report on malaria case management practice at the health facility level, both in lower likelihood of diagnostic testing of suspect malaria cases and elevated use of presumptive treatment. Participation in PPE trainings was associated with higher likelihood of diagnostic testing, and availability of PPE was associated with higher odds of treatment of confirmed cases. Glove availability was associated with lower odds of presumptive treatment. At the patient level, fever was associated with higher likelihood of both presumptive treatment as well as positive treatment.

Malaria diagnostic testing was moderate across studied health facilities, and less than 60% of febrile patients received either microscopy or an RDT for malaria. Treatment for positive cases was high, and the large majority of patients with a positive malaria diagnostic test (85.9%) received an antimalarial drug. Antimalarial drug availability did not appear to be an important independent determinant of positive treatment, though malaria positive patients without fever were less likely to receive antimalarial drugs than those with fever. Antimalarial drugs were provided presumptively to 15.8% of patients, but presumptive treatment was inadequate to cover the 38.1% of febrile patients that did not receive a malaria diagnostic test.

At the district level, it appeared that location in an EVD-affected zone compared to an unaffected zone was not significantly associated with malaria case management practices at health facilities. This suggests that changes in case management practices as a result of the EVD epidemic may not have taken place across entire zones or health districts. This hypothesis is supported by the strong observed associations between facility-level factors and likelihood of diagnostic testing, presumptive treatment, and positive treatment.

The strong observed association between EVD case report and malaria case management practices suggests that first-hand contact with an EVD patient, whether confirmed or suspected, had an important influence on the ways that health workers managed suspect malaria cases. Where health facilities had received an EVD patient, health workers at that facility appeared to be much less likely to perform a diagnostic test on febrile patients and much more likely to presumptively treat any patient with antimalarial drugs without doing a diagnostic test. If a suspect malaria patient actually has EVD, performing a blood draw for a malaria diagnostic test could put the health worker at higher risk for EVD (4). Health workers who had seen or thought they had seen EVD cases at their facility may have been more aware of the risk of EVD infection associated with close patient contact and therefore more inclined to presumptively treat suspect malaria cases rather than perform malaria diagnostic tests which require close patient contact and blood draws.

Presumptive treatment of suspect malaria cases is normally discouraged by Guinean policy which requires diagnostic confirmation of all suspect malaria cases (2). However, presumptive treatment may reduce the risk of nosocomial transmission and health worker EVD infection if health facilities do not have adequate PPE to perform malaria diagnostic tests (4). Increased presumptive treatment at facilities that had seen an EVD case may therefore have been protective against EVD transmission risk associated with malaria diagnostic testing. However, health facilities that had not seen first-hand a suspected EVD

case were less likely to presumptively treat suspect malaria cases and more likely to perform malaria diagnostic tests. This would have made those health workers more vulnerable to EVD transmission in the event of an EVD patient presenting to the health facility. Health workers faced up to 100 times greater risk for EVD transmission than the general population during the EVD epidemic (18). Proactive, preventative approaches to patient care and risk-reduction should therefore be stressed as the epidemic continues, especially in facilities which have not already had first-hand experience with EVD cases.

PPE training was positively associated with malaria diagnostic testing, and if adequate PPE was available, health workers appeared to be more likely to treat diagnostically-confirmed patients with antimalarial drugs. This would have reduced infection risk while increasing the likelihood that malaria patients would receive appropriate treatment. However, only 6.2% of all facilities had complete PPE available at time of survey. Although these data do not actually represent the availability of PPE at the time that patients were seen at health facilities, it is likely that a large proportion of diagnostic test were performed in the absence of complete PPE. If gloves were available, health workers also appeared to be less likely to presumptively treat patients with antimalarial drugs. In the absence of full PPE, however, only gloves would not have been adequate to safely perform a malaria diagnostic test for patients with (4).

Fever was the only individual-level factor that appeared to be significantly associated with malaria case management practices at Guinean health facilities. The likelihood of both presumptive treatment and positive treatment were higher for patients who had fever compared to those who did not. Elsewhere patient history of fever has been shown to be a significant predictor of antimalarial prescription practice among health workers (40). The influence of fever on presumptive treatment likelihood may have been important for reducing malaria comorbidity in EVD patients. In Conakry, Guinea's capital, up to 70% of

EVD patients also had malaria (23). Presumptive fever treatment with antimalarial drugs may therefore have reduced malaria comorbidity in a high proportion of EVD-positive patients.

Whereas more than 70% of health workers in EVD-affected districts reported participation in EVD, PPE and malaria case management trainings, less than 50% of health workers in unaffected districts reported participation in any of these trainings. Absent or ineffective infection control practices in health facilities are posited as major amplification points of transmission in the early part of the epidemic (16, 18). Predictably, response efforts and trainings focused on the most highly affected districts. However, this likely left health facilities in unaffected districts ill-prepared to handle potential introduction of EVD cases and provide effective case management to malaria cases in the context of possible EVD transmission.

Our ability to measure of the appropriateness of malaria case management of febrile patients was limited by the lack of national guidelines during the EVD epidemic and we were unable to account for point availability of PPE or the correctness of the antimalarial drugs prescribed. Using 2014 WHO recommendations for diagnostic testing or presumptive antimalarial treatment of all fever cases, though, we were able to conservatively categorize malaria case management practices in November 2014. Lack of presumptive treatment, antimalarial drug prescription for negative diagnostic tests, and no treatment for positively confirmed cases were major causes of mismanagement of febrile cases. The relatively high rate of mismanagement of fever cases (31.5%) could have important consequences on excess malaria morbidity and mortality. Untreated or incorrectly managed malaria has a low but important probability of progressing to severe disease, and the mortality risk for patients with untreated severe malaria is 60-73% (41).

As of April 2015, the EVD outbreak continues in Guinea and other surrounding countries (10). Although national malaria case management guidelines were standardized were being disseminated as of February 2015 (36), the information presented here has important implications for ongoing information dissemination efforts trainings. As the EVD epidemic continues, health workers who have not had first-hand experience with suspected EVD cases may be more likely to continue malaria case management practices such as diagnostic testing which, in the absence of adequate PPE, may put them at elevated risk of EVD infection. Training efforts may therefore focus on the importance of presumptive malaria treatment to limit EVD transmission when adequate PPE is unavailable. When the EVD epidemic is over, however, facilities that have actually received suspect EVD case(s) may require special communication efforts to harmonize their malaria case management practices with original case management guidelines which typically discourage presumptive treatment. The NMCP may also consider a facility's access to PPE as an important determinant of that facility's case management practices and target malaria case management trainings accordingly.

This analysis faced several limitations. Individual patient data was only abstracted for November 2014 and November 2013. It is therefore difficult to extrapolate to actual case management practices across the whole course of the epidemic. Case management practices in August when the Ebola epidemic was at its peak could have been quite different than in November, for example. Because of limitations in the survey design, we were also unable to examine temporal associations between the time that a health facility reported having actually received a suspect EVD case and any changes in malaria case management practices in the weeks immediately following that report. Additionally, EVD case report by health workers was not verified with actual patient records. We were therefore unable to further examine why a small proportion of facilities in EVD-unaffected zones reported having received EVD cases. The perception of having received an EVD case

nevertheless appeared to be a significant determinant of malaria case management practices among health workers.

The other major limitation of this study was the lack of data on other possible determinants of malaria case management practices. Health worker position (doctor versus nurse) and years of experience are predictors of case management practices for malaria patients (28). Because our data were retrospectively abstracted from patient registers, provider-level data was not available for each patient and therefore not included in our analyses. Another important covariate that could not explicitly be measured in this analysis was the existing guidelines on malaria case management practice. Numerous attempts were made to catalogue timing and location of malaria case management guidelines over the course of the Ebola epidemic. These attempts were not successful, however, likely because records were not systematically kept on the issuance of guidelines. Personal conversations with NMCP and CDC staff suggested that the dissemination of malaria case management guidelines was sporadic and incomplete until February, 2015 and likely played a negligible role in determining actual case management practice in Guinean health facilities (36).

The lack of patient outcome data is another important limitation of this study. In most cases, malaria outcomes were not recorded on health facility registers in November 2014. We were therefore limited to discussing recorded malaria case management practices. It may be possible to model patient outcomes from correct and incorrect malaria case management based on previous epidemiological efforts and modeling efforts, however (41).

Conclusion

The ongoing EVD epidemic in Guinea and surrounding countries in West Africa has been characterized by high rates of nosocomial infection, and health workers are at nearly 100 times higher risk of infection than the general population (18). Malaria morbidity and mortality in Guinea has also increased due to drastic declines in treatment seeking (21), and problems in differentiating EVD versus suspect malaria cases complicate malaria case management (4). The rainy season and accompanying period of high malaria transmission is approaching in May, and EVD transmission persists in parts of the country (39). Information about malaria case management practices at health facilities and determinants of those factors is needed to reduce EVD transmission risk at health facilities while limiting excess malaria morbidity and mortality from incorrect case management.

We saw moderate rates of malaria diagnostic testing and insufficient presumptive treatment for febrile cases at health facilities in November 2014. Malaria case management practices were highly associated with whether a facility reported having received a suspect EVD case, suggesting a reactive effect of personal exposure to EVD patients on health workers' malaria case management practices. Although this may have had a protective effect for health workers at health facilities who had seen cases of EVD, workers at health facilities which did not report having received EVD case(s) were more likely to continue case management practices which could put them at heightened risk for the epidemic. Although availability of PPE was associated with increased likelihood of diagnostic testing and treatment of positive cases, less than 7% of surveyed facilities reported complete PPE availability at the time of the survey. A large majority of malaria diagnostic tests performed in November 2014 were likely done in the absence of adequate equipment to prevent EVD transmission.

As the Guinean NMCP prepares for the 2015 high malaria transmission season, careful consideration must be taken to reduce the risk of health worker infection from EVD and

limit excess malaria morbidity and mortality in the context of the EVD epidemic. As the EVD epidemic continues, the NMCP may focus training efforts on unaffected facilities to emphasize the importance of presumptive malaria treatment when adequate PPE is unavailable in order to reduce EVD transmission risk associated with malaria diagnostic testing. After the end of the EVD epidemic, however, special attention may be placed on facilities that reported having seen EVD case(s) in order to reemphasize the importance of diagnostic confirmation of all suspect malaria cases. Care should also be taken to reduce the number of febrile patients who neither receive a malaria diagnostic test nor presumptive treatment, because this group is likely at much higher risk for increased morbidity and mortality from untreated malaria.

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Tables & Figures

Tables

Table 1

Table 1. Characteristics of Surveyed Health Facilities in Guinea by Ebola-affected Versus Unaffected Zone, November 2014

	Ebola-affected n= 55 n (%)	Unaffected n=58 n (%)	*P*-val	Total n=113 n (%)
Facility Type				
Health Centers	26 (47.0%)	24 (41.4%)	0.61	50 (44.2%)
Hospitals	8 (14.5%)	7 (12.1%)	0.81	15 (13.3%)
Health Posts (ref)	21 (38.2%)	27 (46.5%)		48 (42.5%)
RDT Availability[a]	42 (76.0%)	46 (79.3%)	0.66	88 (77.8%)
Antimalarial Drug Availability[a]	40 (72.7%)	42 (72.4%)	0.67	82 (72.6%)
PPE Availability				
Gloves[a]	42 (76.4%)	47 (81.0%)	0.39	89 (78.8%)
Complete PPE [b]	6 (10.9%)	1 (1.7%)	<0.001	7 (6.2%)
Malaria Trainings	49 (89.1%)	23 (39.7%)	0.003	72 (63.7%)
EVD Trainings	44 (80.0%)	16 (27.6%)	<0.001	60 (53.1%)
PPE Trainings	45 (81.9%)	26 (44.8%)	<0.001	71 (62.8%)
Facilities Reporting EVD case(s)	17 (30.9%)	5 (8.6%)	0.005	22 (19.5%)

[a] ≥ 100% of monthly commodity consumption average available at time of survey

[b] Reported availability of gloves, apron, boots, helmet, and face screen at time of survey

Note: Results are unweighted

Table 2

Table 2: Demographic and Case Management Characteristics of Patients at Guinean Health Facilities, by Ebola-affected Versus Unaffected Zone, November 2014 (N=3,726)

	Ebola-affected % n= 1870	Unaffected % n= 1856	*P*-val	Total % n= 3,726
Patients ≥ 5 years old	53.1	70.7	0.007	61.1
Febrile Patients	60.3	63.8	0.324	61.9
Diagnostic Test for Fever	52.7	65.2	0.256	58.8
Antimalarial treatment	42.8	44.3	0.740	43.5
Presumptive [a]	14.3	17.5	0.419	15.8
Positive [b]	91.1	80.8	0.092	85.9

Note: Results are unweighted

[a] Presumptive: Presumptive antimalarial prescription without prior diagnostic confirmation

[b] Positive: Antimalarial prescription after positive diagnostic confirmation

Table 3

Table 3. Factors Associated with Malaria Diagnostic Testing for Febrile Patients in Guinean Health Facilities, November 2014 (N=2,436)

	Unadjusted Odds Ratio (OR)	95% CI	*P*-val	Adjusted Odds Ratio (aOR)	95% CI	*P*-val
District-level						
EVD Affected Zone	0.58	0.25, 1.34	0.20	2.82	0.42, 19.0	0.29
Facility-level						
EVD Case Report	0.35	0.14, 0.91	0.03	0.01	0.001, 0.11	<.0001
PPE Availability						
Gloves	1.35	0.55, 3.28	0.51	5.58	0.99, 31.3	0.051
Complete PPE	4.58	0.99, 21.2	0.05	2.88	0.62, 13.5	0.18
Malaria Trainings	1.01	0.19, 5.43	0.99	0.41	0.09, 1.86	0.25
EVD-related Trainings						
EVD	1.12	0.40, 3.18	0.83	1.07	0.19, 6.10	0.94
PPE	1.19	0.46, 3.04	0.72	5.63	1.88, 16.9	0.00
Patient-Level						
Age ≥ 5 years old	1.24	0.80, 1.93	0.33	0.60	0.29, 1.26	0.18
Confounders						
RDT availability	0.98	0.30, 3.13	0.97	0.43	0.05, 3.41	0.42
Facility Type						
Health Center	1.79	0.75, 4.29	0.19	0.73	0.14, 3.75	0.71
Hospital	0.23	0.14, 0.37	<.0001	3.44	0.68, 17.4	0.13
Health Post (ref)						
Diagnostics, 2013 [a]	2.71	1.48, 4.94	0.001	1.18	0.49, 2.86	0.71

Note: Results are weighted

[a] Diagnostics, 2013: Malaria diagnostic testing for febrile patients in November, 2013

Table 4

Table 4. Factors Associated with Presumptive Antimalarial Treatment Without Prior Diagnostic Confirmation at Guinean Health Facilities, November 2014 (N=1,767)

	Unadjusted Odds Ratio (OR)	95% CI	*P*-val	Adjusted Odds Ratio (AOR)	95% CI	*P*-val
District-level						
EVD Affected Zone	0.75	0.37, 1.51	0.42	0.36	0.07, 1.85	0.22
Facility-level						
EVD Case Report	1.79	0.89, 3.60	0.10	30.7	2.12, 444	0.01
PPE Availability						
Gloves	0.73	0.28, 1.93	0.53	0.13	0.04, 0.41	0.001
Complete PPE	0.18	0.05, 0.62	0.006	1.32	0.17 10.2	0.79
Malaria Trainings	1.88	0.37, 9.64	0.45	1.92	0.40, 9.11	0.41
EVD-related Trainings						
EVD	0.90	0.37, 2.18	0.81	1.34	0.39, 4.63	0.64
PPE	0.59	0.28, 1.21	0.15	0.37	0.13, 1.09	0.07
Patient-Level						
Age ≥ 5 years old	1.21	0.79, 1.85	0.39	1.60	0.63, 4.02	0.32
Fever	1.74	0.90, 3.37	0.10	2.28	1.17, 4.46	0.02
Confounders						
Antimalarial availability	0.30	0.14, 0.64	0.002	0.09	0.03, 0.27	<.0001
Facility Type						
Health Center	0.55	0.27, 1.14	0.11	0.51	0.19, 1.41	0.20
Hospital	3.20	2.14, 4.80	<.0001	<0.001	<0.001 <0.001	<.0001
Health Post (ref)						
Presumptive, 2013 [a]	2.59	1.60, 4.18	<.0001	1.32	0.63, 2.76	0.46

Note: Results are weighted

[a] Presumptive, 2013: Presumptive treatment trends in November, 2013

Table 5

Table 5. Factors Associated with Antimalarial Treatment After Positive Diagnostic Confirmation at Guinean Health Facilities, November 2014 (N=1,345)

	Unadjusted Odds Ratio (OR)	95% CI	*P*-val	Adjusted Odds Ratio (AOR)	95% CI	*P*-val
District-level						
EVD Affected Zone	2.68	0.89, 8.06	0.08	0.79	0.18, 3.51	0.76
Facility-level						
EVD Case Report	1.49	0.34, 6.46	0.60	1.69	0.14, 21.0	0.69
PPE Availability						
Gloves	0.81	0.27, 2.41	0.70	3.44	0.66, 18.0	0.14
Complete PPE	56.19	4.28, 738	0.002	29.1	1.23, 688	0.04
Malaria Trainings	6.94	1.47, 32.8	0.01	0.85	0.06, 12.4	0.90
EVD-related Trainings						
EVD	5.95	1.80, 19.7	0.004	2.43	0.17, 34.4	0.51
PPE	3.29	1.05, 10.4	0.04	1.05	0.12, 9.49	0.96
Patient-Level						
Age ≥ 5 years old	0.49	0.25, 0.97	0.04	1.08	0.41, 2.87	0.88
Fever	2.59	1.00, 6.68	0.05	8.30	3.20, 21.5	<.0001
Confounders						
Antimalarial availability	2.31	0.34, 15.5	0.39	0.36	0.04, 3.31	0.37
Facility Type						
Health Center	2.71	0.70, 10.5	0.15	4.05	0.68, 24.2	0.12
Hospital	0.05	0.02, 0.11	<.0001	>999	>999, >999	<.0001
Health Post (ref)						
Pos Treatment, 2013 [a]	1.07	0.39, 2.90	0.90	2.23	0.92, 5.44	0.08

Note: Results are weighted

[a] Pos Treatment, 2013: Antimalarial treatment of diagnostically confirmed malaria cases, November 2013

Figures

Figure 1

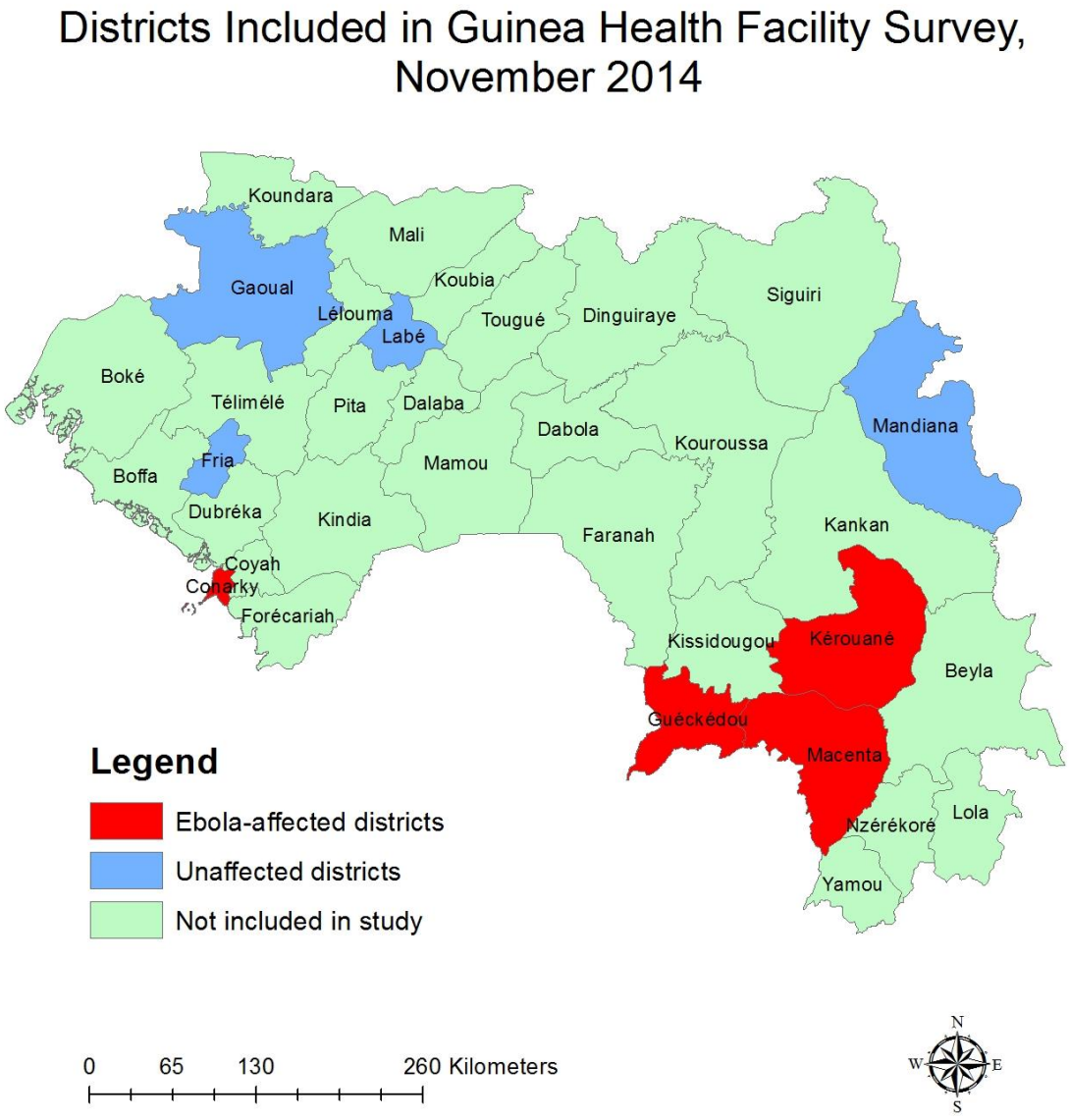


Figure 2

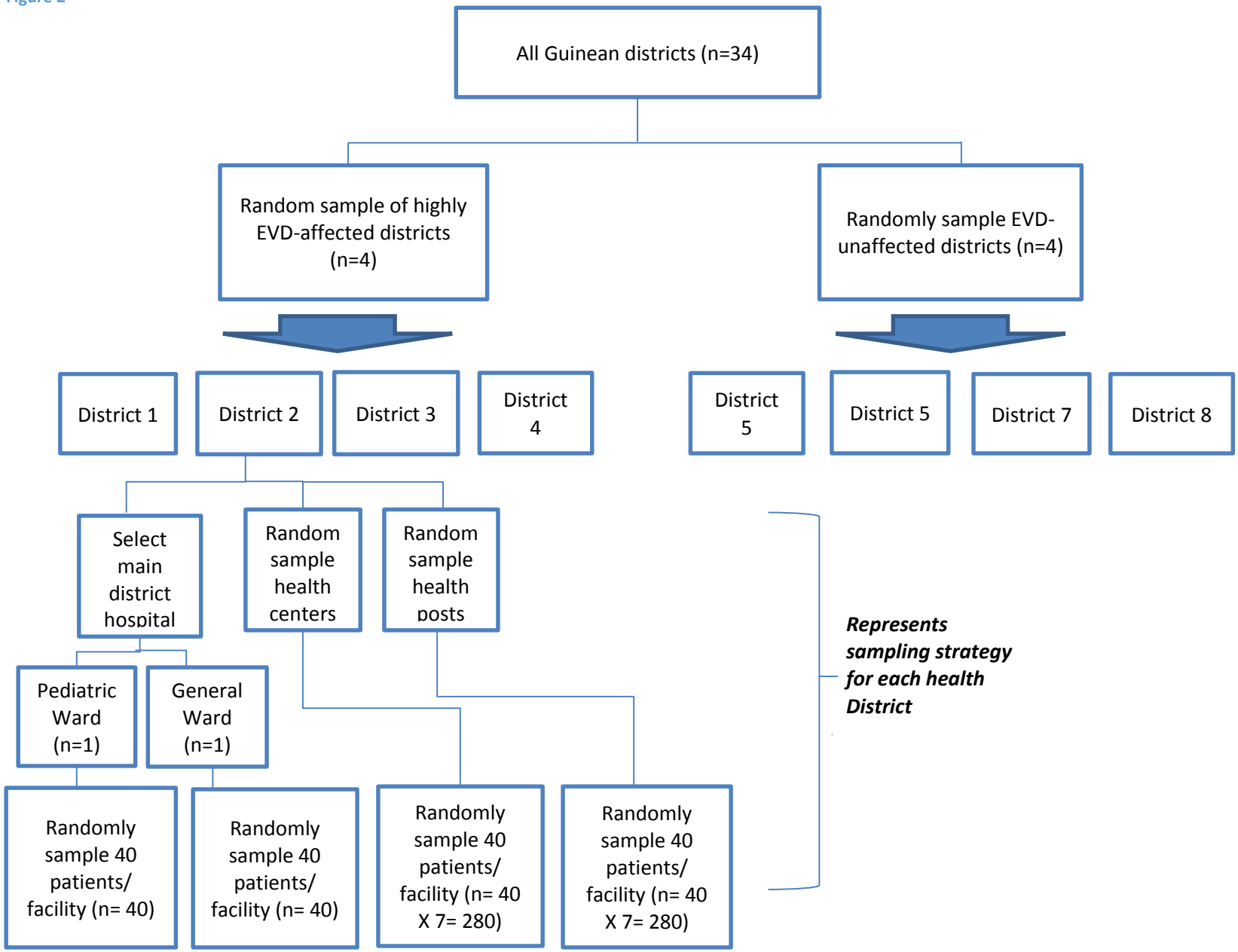
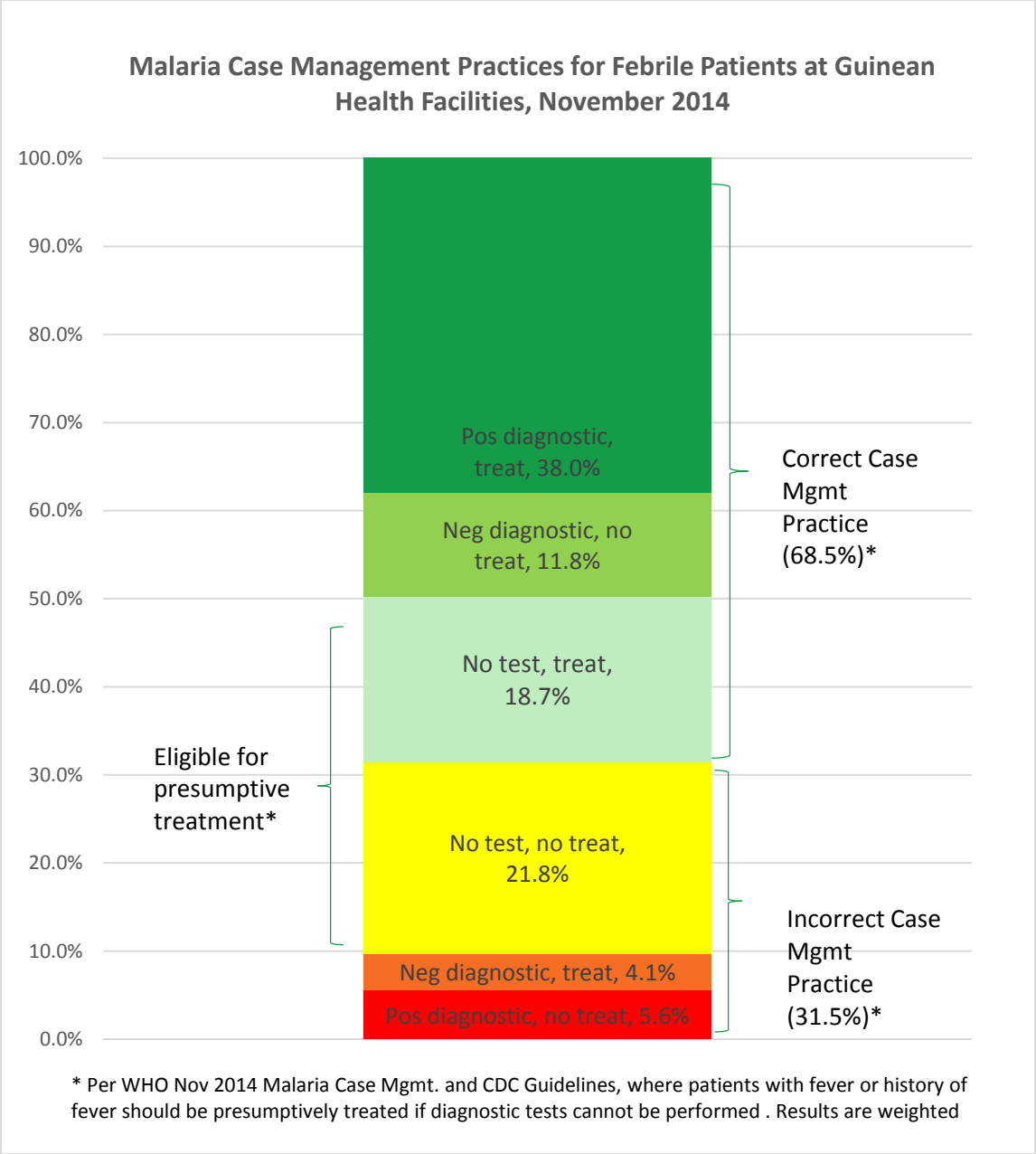
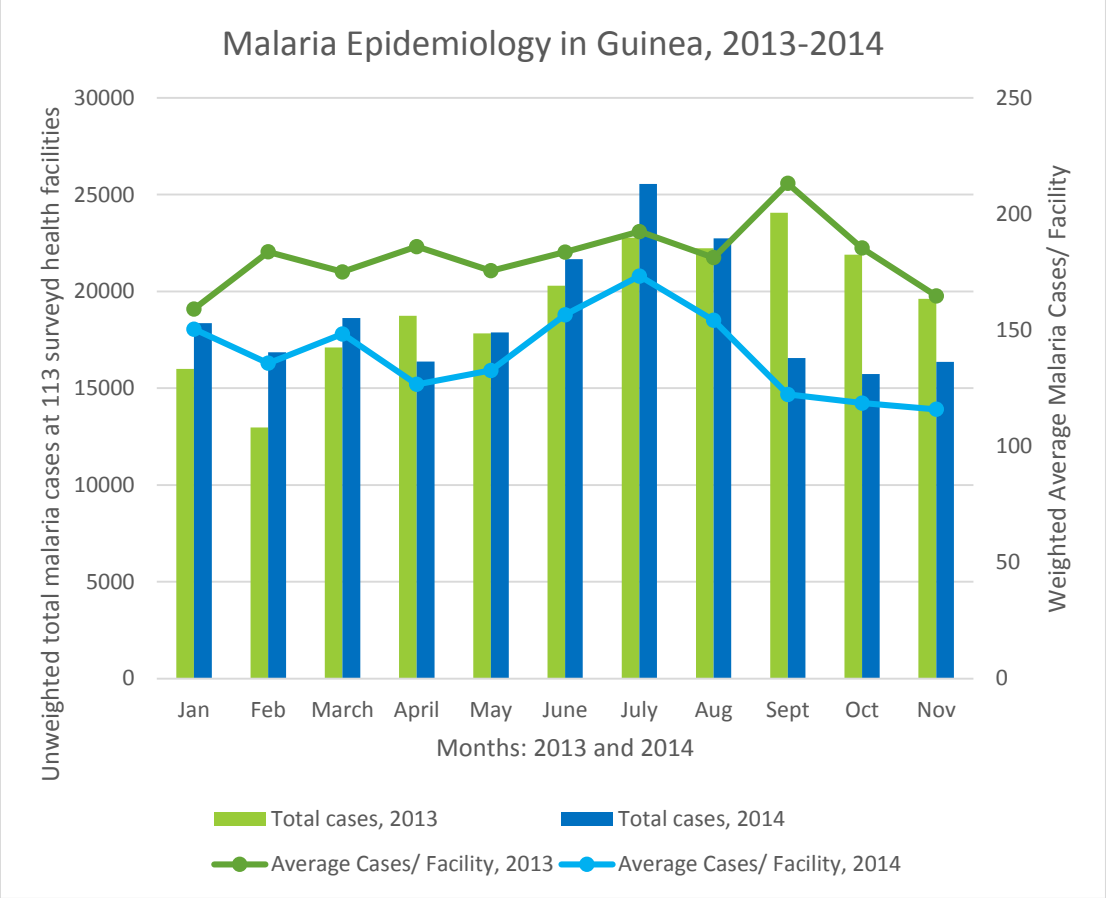

All Guinean districts (n=34)
Random sample of highly EVD-affected districts (n=4)
Randomly sample EVD-unaffected districts (n=4)
District 1
District 2
District 3
District 4
District 5
District 5
District 7
District 8
Select main district hospital
Random sample health centers
Random sample health posts
Pediatric Ward (n=1)
General Ward (n=1)
Randomly sample 40 patients/ facility (n= 40)
Randomly sample 40 patients/ facility (n= 40)
Randomly sample 40 patients/ facility (n= 40 X 7= 280)
Randomly sample 40 patients/ facility (n= 40 X 7= 280)
Represents sampling strategy for each health District

Figure 3



* Per WHO Nov 2014 Malaria Case Mgmt. and CDC Guidelines, where patients with fever or history of fever should be presumptively treated if diagnostic tests cannot be performed . Results are weighted

Figure 4


Malaria Epidemiology in Guinea, 2013-2014
Unweighted total malaria cases at 113 surveyd health facilities
Weighted Average Malaria Cases/ Facility
30000
25000
20000
15000
10000
5000
0
250
200
150
100
50
0
Jan
Feb
March
April
May
June
July
Aug
Sept
Oct
Nov
Months: 2013 and 2014
Total cases, 2013
Total cases, 2014
Average Cases/ Facility, 2013
Average Cases/ Facility, 2014

Chapter III: Summary, Public Health Implications, Possible Future Directions

Summary

Here we describe the results of a retrospective register abstraction and health worker questionnaire conducted in Guinea in December 2014. We examined malaria case management practices at health facilities in November 2014 and factors associated with those practices. Because malaria and EVD have similar initial clinical presentations and both diseases require blood draws or pricks for diagnostic confirmation, case management of malaria in the context of the EVD is extremely complicated. Health workers may be at a heightened risk of EVD transmission because of close patient contact and blood draws associated with malaria diagnostic testing, and mismanagement of malaria cases may result in excess malaria morbidity and mortality. The data presented in this study may therefore be useful to policy makers to support efforts to reduce excess malaria morbidity and mortality and reduce EVD transmission risk among health workers.

Using 2014 WHO temporary guidelines for malaria case management in EVD-affected countries, we found relatively high rates of malaria mismanagement. A high percentage (21.8%) of fever cases received neither a malaria diagnostic test nor presumptive malaria treatment. Treatment of negative patients or no treatment for positively confirmed cases were also relatively common. Because data were not collected on the availability of PPE for each diagnostic test performed at the time of patient visit, we were unable to measure what proportion of diagnostic tests was performed in the presence of adequate PPE. The low reported availability of complete PPE however (6.2%), suggests that a high proportion of malaria diagnostic tests were performed in the absence of adequate protective equipment.

We found whether a health facility reported having received EVD case(s) was highly associated with malaria case management practices. EVD transmission risk associated with malaria diagnostic testing may have been mitigated by a switch to presumptive treatment in facilities which had seen EVD case(s). Continued diagnostic testing of febrile cases at facilities which had not already reported EVD cases, however, may have put those health workers at higher transmission risk in the event of EVD introduction. PPE training and availability of PPE appeared to have the opposite effect; febrile patients at health facilities which had received PPE trainings were more likely to receive a malaria diagnostic test, and patients at facilities with full PPE availability were more likely to be treated for positively confirmed malaria.

Public Health Implications

The 2015 rainy season and corresponding high malaria transmission season is quickly approaching in Guinea. Meanwhile EVD transmission continues in the west of the country and areas around the capital. As of April 5th, 2015, one prefecture that was originally included as an unaffected prefecture in this study had reported at least 4 confirmed cases (42). Policy makers need therefore to focus on ways to reduce excess malaria morbidity associated with the EVD epidemic and reduce EVD infection risk among health workers.

Efforts are under way in Guinea to counter these challenges. The Guinean NMCP finalized national guidelines for malaria case management in February, 2015. These guidelines are currently being disseminated, and health workers around the country are participating in malaria and EVD trainings. A new program is also being planned that will provide mobile malaria care and supervision in rural communities at monthly intervals throughout the 2015 rainy season. The program aims to reverse the immense drop in malaria treatment

seeking that was observed in 2014 through increased malaria care provision and community mobilization efforts to restore faith in the health system.

The results presented in this paper support efforts to reduce malaria morbidity and mortality and reduce EVD infection risk among health workers during the 2015 high malaria transmission season in Guinea. Policy makers may use the findings to target specific facilities and districts for reinforced training or information dissemination efforts. Facilities that have seen EVD cases, for example, are much less likely to diagnostically confirm suspect malaria cases and much more likely to presumptively treat. Although this may be advantageous as long as the EVD epidemic persists, these facilities may require extra training after the EVD epidemic in order to harmonize their case management practices with national guidelines. If the EVD epidemic continues and the Guinean NMCP continues to prioritize presumptive treatment, however, then policy makers may instead focus on unaffected facilities and emphasize the utility of presumptive treatment in order to minimize EVD transmission risk.

We also found relatively high rates of inappropriate case management of febrile cases. Inappropriate malaria case management, whether through antimalarial prescription to negative cases or lack of antimalarial prescription to positively confirmed cases, likely increases malaria morbidity and mortality. In the context of the EVD epidemic, inappropriate case management also includes lack of presumptive treatment for febrile cases who do not receive a malaria diagnostic test. Ongoing malaria trainings and information dissemination efforts may therefore target these causes of inappropriate malaria case management in order to decrease excess malaria morbidity and mortality during the ongoing EVD epidemic.

Possible Future Directions

This study lends itself to a variety of avenues for further research. One obvious next step is the replication of this study in other EVD-affected countries. Compared to Guinea, Liberia and Sierra Leone saw much higher rates of health facility closures during the peak of the EVD epidemic in 2014. This likely had profound public health effects. Further research could therefore explore the effects of the EVD epidemics in Liberia and Sierra Leone on malaria case management and treatment seeking. CDC and the Liberian NMCP are currently drafting a protocol to undertake this study.

Another important area of possible study is patient perceptions of care seeking in the context of the EVD epidemic. There has been speculation that the drastic drop in malaria treatment seeking observed in 2014 was due to patients' reluctance to attend health facilities because of fears of contracting EVD. However, little research has actually focused on patient experience and reasons for or for not frequenting health facilities. This type of research could shed light on these important issues and prove valuable in ongoing efforts to rebuild and restore faith in devastated health systems in Guinea and surrounding countries. The input of social and behavioral scientists would contribute valuably to the development of subsequent study protocols.

Finally, this research has important implications for preparation and response efforts for future epidemics. The current EVD epidemic has been a lesson in how unprepared many health systems are to deal with infectious disease outbreaks. It has also demonstrated how secondary public health consequences of such an outbreak may far surpass its immediately observable effects. Understanding of the main drivers of health worker practice will support efforts to mitigate primary and secondary public health consequences in the event of a future epidemic on the scale of the 2014-2015 West Africa EVD epidemic.

Appendices

Appendix I: Register Abstraction Tools for Nov 2013 and Nov 2014

District Sanitaire:_____ ID de Structure Sanitaire : _____

Service_____

2013 : Vérification du Registre d'Novembre 2013 (Cochez la cage correspondante)												
		Age				Résultat du Test				Traitement Antipaludique		
	Fièvre	< 5 ans	≥ 5 ans	Femme Enceinte	Testé	TDR +	TDR -	GE+	GE-	CTA	Quinine Inj/ Arte. Inj	Autre
1												
2												
3												
4												
5												
6												
7												
8												
9												
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11												
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40												

District Sanitaire:_____ ID de Structure Sanitaire :_____

Service :_____

2014 : Vérification du Registre d'Novembre 2014 (cochez la cage correspondante)												
		Age				**Résultat du Test**				**Traitement Antipaludique**		
	Fièvre	**< 5 ans**	**≥ 5 ans**	**Femme Enceinte**	**Testé**	**TDR +**	**TDR -**	**GE+**	**GE-**	**CTA**	**Quinine Inj/ Arte. Inj**	**Autre**
1												
2												
3												
4												
5												
6												
7												
8												
9												
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Appendix II: Aggregate Register Abstraction Form

		2013											2014										
		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov
Adults	All cause consultations																						
	Fever cases																						
	Malaria diagnostic tests performed (RDT or microscopy)																						
	Confirmed malaria cases																						
	ACTs prescribed																						
	IV quinine or IV artesunate prescribed																						
Children <5	All cause consultations																						
	Fever cases																						
	Malaria diagnostic tests performed (RDT or microscopy)																						
	Confirmed malaria cases																						
	ACTs prescribed																						

	IV quinine or IV artesunate prescribed																						
Pregnant women	Number of pregnant women seen at ANC																						
	Doses of SP administered to pregnant women																						

Appendix III: Health Worker Questionnaire

Date: I__I__I-I__I__I-__I__I
Interviewer ID: _____
Prefecture: _____
ID of Health Facility: _____

A. Information about Respondent

Question/Variable	*Response*	*Instructions:*
1. Position of respondent	1= Clinician 2. Nurse 3. Health Care Technician 4. Pharmacist 5. Midwife 6. Other _____	
1. Sex	1 = Male 2 = Female	
2. How long have you worked in this HF?	1= Less than 6 months 2= Between 6 months and 1 year 3= More than 1 year	*If 1, skip to Section C*
3. In your job, do you consult patients with fever?	1= Yes 2= No	*If 2, thank respondent for participating, end survey, and start new survey with another consenting health worker. If 1 continue to part B.*

B. Malaria Case Management: Before Ebola

1. Before the Ebola outbreak, did you or another designated person in the health facility perform RDTs for cases of fever?	1= Yes 2= No	
2. Before the Ebola outbreak, did you or a designated person in the lab perform	1= Yes 2= No	

microscopy for cases of fever?		
3. Before the Ebola outbreak, did you prescribe ACTs for confirmed malaria cases?	1= Yes 2= No	
4. Before the Ebola outbreak, did you ever refer fever cases to a higher-level health facility for treatment?	1= Always 2= Sometimes 3= Never 88 = Do Not Know	
5. Before the Ebola outbreak, did you ever treat fever cases with ACTs <u>without</u> first testing for malaria?	1= Always 2= Sometimes 3= Never 88 = Do Not Know	
6. Before the Ebola outbreak, did you (i.e., this health facility) treat severe malaria cases?	1= Yes 2= No 88 = Do Not Know	
7. Before the Ebola outbreak, did you ever refer severe malaria cases to a higher-level health facility for treatment?	1= Always 2= Sometimes 3= Never 88 = Do Not Know	
8. Before the Ebola outbreak, did you or other health workers in this facility give SP to pregnant women?	1= Yes 2= No 88 = Do Not Know	

C. <u>Malaria Case Management: After Ebola</u>

1. Since the Ebola outbreak, do you or another designated person in the health facility perform RDTs for cases of fever?	1= Yes 2= No	
2. Since the Ebola outbreak, do you or a designated person in the lab perform microscopy for cases of fever?	1= Yes 2= No	

3. Since the Ebola outbreak, do you prescribe ACTs for confirmed malaria cases?	1= Yes 2= No	
4. Since the Ebola outbreak, do you ever refer fever cases to a higher-level health facility for treatment?	1= Always 2= Sometimes 3= Never 88 = Do Not Know	
5. Since the Ebola outbreak, do you ever treat fever cases with ACTs <u>without</u> first testing for malaria?	1= Always 2= Sometimes 3= Never 88 = Do Not Know	
6. Since the Ebola outbreak, do you (i.e., this health facility) treat severe malaria cases?	1= Yes 2= No 88 = Do Not Know	
7. Since the Ebola outbreak, do you ever refer severe malaria cases to a higher-level health facility for treatment?	1= Always 2= Sometimes 3= Never 88 = Do Not Know	
8. Since the Ebola outbreak, do you or other health workers in this facility give SP to pregnant women?	1= Yes 2= No 88 = Do Not Know	

D. <u>Case Management of Suspect Ebola Cases</u>

1. Do you know how to identify suspect cases of Ebola?	1= Yes 2= No	*If 2, skip to Q6*
2. If so, what is the definition of a suspect Ebola case?	1=Fever + notion of contact 2= Fever + at least 2 symptoms (see below) 3=Unexplained bleeding 4 = Other _____ 88 = Do Not Know	*Select all that apply Response should be unprompted*

3. What are the symptoms of Ebola?	1= Fever 2= Headache 3=Vomiting/nausea 4=Diarrhea 5=Abdominal pains 6=Anorexia 7=Fatigue 8= Muscle pains 9= Joints pains 10=Difficulty breathing 11=Hiccups 12=Bleeding 13=Other _____ 88= Do Not Know	*Select all that apply Response should be unprompted and interviewer should probe for additional responses twice (i.e., « anything else ? »*
4. What should you do for a suspect case of Ebola?	1= Take a blood sample 2= Refer to central hospital 3= Refer to Ebola treatment center 4=Refer to transit center 5= Refuse to see patient 6= Treat patient for malaria and refer to Ebola treatment center *if* does not get better in 48 hours 7= Treat patient for malaria and refer to Ebola treatment center immediately 8= Other_____ 88= Do Not Know	*Select all that apply* *Response should be unprompted and interviewer should probe for additional responses twice (i.e., « anything else ? »*
5. How do you differentiate between suspect cases of Ebola and suspect malaria cases?	1= By RDT 2= By notion of contact 3= By symptoms 4= I don't – I treat all fever cases with ACT 5= I don't – I refer all fever cases to an ETU or transit center 6= Other_____ 88= Do Not Know	*Select all that apply* *Response should be unprompted and interviewer should probe for additional responses twice (i.e., « anything else ? »*

6. Have you encountered a patient who was considered a suspect case of Ebola here in this health facility?	1= Yes 2= No 88= Do Not Know	*If 2, skip to Section E*
7. If yes, what did you do?	1= Took blood sample 2= Referred (where?_____) 4= Refused to see patient 5= Treated with ACT 9= Other_____ 88= Do Not Know	*Select all that apply*

E. <u>Training and PPE</u>

1. Have you received information or training on identification and case management of suspect Ebola cases?	1= Yes 2= No	*If 2, skip to Q3*
2. If yes, where did you receive this information?	1= Training 2= Supervisor 3= Online 4= Radio 5= Posters 6= Other_____	*Select all that apply*
3. Have you received information or training on identification and case management of suspect malaria cases?	1= Yes 2= No	*If 2, skip to Q5*
4. If yes, where did you receive this information?	1= Training 2= Supervisor 3= Online 4= Radio 5= Posters 6= Other_____	*Select all that apply*

5. Do you currently have access to personal protective equipment (PPE)?	1= Yes 2= No 88 = Do Not Know	*If 2 or 88, skip to Q7*
6. What kind of PPE do you have access to if you needed it?	1 = Gloves 2 = Gowns 3 = Goggles 4 = Boots 5 = Cap 6 = Face shield 7= Other_____	*Select all that apply*
7. Have you received training within the last 6 months on how to use the PPE?	1= Yes 2= No	*If 2, skip to Q9*
8. If yes, what kind of training did you receive?	1= Special training on how to use PPE with suspect Ebola cases (i.e., from an outside group of trainers) 2= Regular training on infection control for any type of infection 3= Informal training to protect myself (i.e., on site from a DPS supervisor) 4= Other _____	
9. Are there enough gloves at this facility to last for a month (a pair of gloves for each patient)?	1= Yes 2= No 88 = Do Not Know	
10. Estimate how many gloves (pieces, not pairs) there are.	____	Respondent can direct interviewer to someone else who may have this information

F. <u>Observations on Health Care Seeking</u>

1. Have you noticed a change in the volume of patients coming to your HF since the Ebola epidemic?	1= Increase in patients 2= Decrease in patients 3= No change 88 = Do Not Know	*Interviewer may need to prompt, "If so, what kind of change, more or less patients?"*

		If 1, 3, or 88 skip next question; questionnaire is finished.
2. If you've noticed a decrease, what do you think are some possible reasons?	1= The patients fear being infected with Ebola in HF 2=Fever patients do not want to go to HFs 3=The patients fear being referred to an ETU 4=The HFs are closed 5= The population fears health care workers 6=Other_____ _ 88 = Do Not Know	*Select all that apply*

End of Survey. Thank respondent.

Appendix IV: Verbal consent form for health worker questionnaires

Appendix 4 : Health Worker Interview Consent Form

Reading Level : 8.6

Surveyor ID: /E /__/__/

District: /_____/__/__/
(DSE or DS)

Health facility ID: /_____/__/__/
(H, CS or PS)

Respondant ID: /____ /__/__/
(AS or ACS)

République de Guinée
Travail-Justice-Solidarité
National Malaria Control Program (NMCP)
****

Survey on the Impact of the Ebola Epidemic on Malaria Case Management

Verbal Consent Form

December 2014

Verified by supervisor : Signature _____

Date

Day		Month		Year			

Introduction.

"My name is … …….. I work with NMCP. We are interviewing healthcare workers in this district to evaluate the impact of the Ebola epidemic on malaria case management in Guinea.

Confidentiality and Consent.

I would like to ask you some questions on malaria case management in the context of the Ebola epidemic. Your responses will be confidential. Your name will not be written on the form and no link will be made between what you say and your name. You are not required to reply to any question that you do not want to. You can stop answering at any point. Your participation is voluntary. Your participation does not pose any risk. We ask you to reply honestly so that we can better understand the effect of the Ebola epidemic on malaria case management. We appreciate your help by answering these questions. You will not be paid for your participation in this study but your participation will help the NMCP to minimize the effects of the Ebola epidemic on malaria case management. The interview will last around 30 minutes. Do you accept to participate?

I certify that the interviewee has been informed of the nature and purpose of the study and that he or she has given their verbal consent to participate in this study.

Date

Day		Month		Year			

_____

Interviewer's signature