Children's anemia levels in West Africa:
a good proxy for malaria morbidity?

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Abstract. Malaria is a major cause of morbidity and mortality in young children in sub-Saharan Africa. Major public health initiatives, such as the Roll Back Malaria program, have made it a global health priority to improve the malaria situation in the next decade. In Africa, however, routine health information is not available to monitor progress on reducing malaria morbidity. The objective of this paper is to examine the utility of using child hemoglobin measures collected in population-based studies as an indicator to monitor changes in the malaria situation. A logistic regression analysis models the effects of malaria prevalence on the probability of serious anemia (Hb<8 g/dl) while controlling for child nutrition and other factors hypothesized to relate to anemia. Individual-level information on children age 6-59 months in five sub-Sahara African countries includes geospatially linked data from three sources: child health and socio-demographic information from the Demographic and Health Surveys (DHS); malaria prevalence estimates from the Mapping Malaria Risk in Africa (MARA) project; and urban extent measures from the Global Rural-Urban Mapping Project (GRUMP). Findings indicate that children in areas of moderate malaria prevalence run the highest risk of serious anemia. These findings are not unlike findings from previous studies, and plausible explanations are presented. Hemoglobin measures are *reliable* measures of anemia (and if untreated, anemia is an almost inevitable outcome of malaria especially in children 6-23 months); the *validity* of hemoglobin measures depends on whether or not the anemia test takes place in malaria transmission season.

INTRODUCTION

The distribution of malaria endemicity in Africa comprises an almost solid belt stretching across sub-Saharan West and Central Africa. Ninety percent of all malaria deaths have occurred among persons living within this area, and most of these deaths have been of children under age five years (WHO 2002). Snow *et al*. (1999a) estimates that approximately 1 million persons in Africa died in 1995 from *Plasmodium falciparum* infection (the malaria parasite transmitted by the most widespread and effective malaria vector, *Anopheles gambiae*), with at least 78 percent of these being child deaths. Although difficult to quantify with certainty, there is evidence that malaria-attributable deaths may contribute to at least 20 percent of all child deaths in Africa (WHO 2002, Korenromp *et al.* 2003, Black *et al.* 2003). Furthermore, for every child who dies of malaria there are at least two more who diagnosed with a clinically defined attack, and a far greater number again who suffer from symptoms of *P falciparum* infection (e.g. fever, frisson, headache, body pains and diarrhea) (Snow *et al*. 1999a).

Demographic surveillance systems provide evidence that malaria mortality risks have increased in the 1990s, due in large part to increased resistance of the malaria parasite to antimalarial drugs (WHO/UNICEF 2003, WHO 2002, Snow *et al*. 2001, Ekvall *et al.* 1998). Major public health initiatives, such as The Global Fund to Fight AIDS, Tuberculosis and Malaria, have prioritized improving the malaria situation in the next decade. Likewise, the Roll Back Malaria program aims to halve malaria-associated morbidity and mortality between 2000 and 2010, with an emphasis on strengthening health services to provide effective treatment and prevention strategies (Nabarro & Taylor 1998). One of the U.N.'s Millennium Development Goals includes a pledge to halt and begin to reverse the incidence of malaria and other major diseases between 1990 and 2015 (Millennium Assembly of the United Nations 2000).

A variety of monitoring strategies is necessary to make available more precise data and assemble indicators needed to monitor progress towards these goals (Cibulskis *et al*. 2002). In Africa, routine health information and vital statistics do not furnish needed information, nor do many health facilities

have the proper tools and trained personnel to diagnose the disease. Furthermore, the majority of deaths attributable to malaria occur at home so they are never officially registered, and only a small fraction of persons with symptoms visit a health care facility (Breman 2001). In view of these data inadequacies which have no short-term solutions, this paper examines the utility of using population-based measures of hemoglobin as one strategy to monitor changes in the malaria situation.

Serious anemia as an indicator for malaria burden

Anemia is defined as hemoglobin (Hb) level below an established threshold, and the lower the cutoff the more severe is the anemia (DeMayer *et al*. 1989). Anemia is a multifactorial condition caused by dietary deficiencies (e.g. lack of iron, folic acid and other micronutrients), helminth infections and other infectious diseases, and blood disorders such as sickle cell anemia, a mutation of the oxygen-carrying hemoglobin protein (Menendez *et al.* 2000). While in developed countries iron deficiency is the most common cause of anemia, in lesser developed countries other factors play a larger role. In countries that are highly malaria endemic, such as those in sub-Saharan Africa, malaria is the main etiological agent responsible for lowering hemoglobin levels and causing anemia (Fleming 1981, Menendez *et al.* 1997).

Hemoglobin measures are proposed as a fitting indicator for tracking the burden of malaria for several reasons. The first reason follows the logic that although not all anemia is caused by malaria (or malaria alone), almost all children with malaria will inevitably develop anemia (Phillips *et al*. 1986). The second reason is because hemoglobin measures are becoming more widely available from population-based surveys. For the past decade, Demographic and Health Surveys increasingly collect this biomarker data using the portable HemoCue photometre (www.hemocue.co.uk). This methodology offers measures with a high level of precision. By definition, the mean Hb measure will fall within a range of plus or minus two times the standard error of the mean in 95 percent of all possible samples of identical size and design. The standard errors for Hb distributions in this study are small: Burkina Faso 8.83 g/dl, SE 0.032; Benin 9.39 g/dl, SE 0.036; Cameroon 10.09 g/dl, SE 0.029; Ghana 9.74g/dl, SE 0.030; and Mali 9.22 g/dl, SE 0.037. Finally, malaria deaths are, statistically speaking, a rarer event than malaria morbidity, and thus more difficult to detect changes in levels. An indicator or proportions of young children with severe anemia, rather than proportions that have died, is a more accessible measure of the burden of malaria (Owusu-Agyei 2002).

The causal mechanisms between anemia and malaria are quite complex but well understood by physiologists (Nestel & Davidsson 2002). In simple terms, malaria causes anemia both by rupturing red blood cells and by suppressing the production of new red blood cells. Hemoglobin is the oxygen-carrying protein in red blood cells so hemoglobin levels will fall to the extent that red blood cells fail to exist. If anemia is severe enough, it carries a significant risk of death by profound hypoxia and congestive heart failure, or more rarely, by cerebral malaria (Philips and Pasvol 1992, English *et al*. 1996). When the *P falciparum* parasite causes hemoglobin levels to fall below the defined cutoff then it is called malaria anemia. The WHO defines severe malarial anemia as a Hb concentration of <5 g/dl in the presence of *P falcipaum* parasitemia of density >10,000 (Warrell *et al*. 1990), although in practice it is usually defined as Hb levels below 'normal' in the presence of malaria infection of any density.

Because anemia is a multifactorial condition, it is not possible to completely isolate the contribution of malaria to anemia simply by measuring hemoglobin. Parasitemia testing is needed to positively identify a *P falciparum* infection, and further testing to diagnose other causes (such as iron deficiency, sickle cell, etc.). However, numerous community-based epidemiological studies have used empirical data to document the causal link between malaria and anemia in malaria-endemic areas, especially in young children and pregnant women (Slutsker *et al.* 1994, Biemba *et al.* 2000, Staubli *et al.* 2001). Korenromp *et al*. (2004) conducted a systematic review of the impact of malaria interventions (insecticide treated bednets, malarial prophylaxis, and insecticide residual spraying) on hemoglobin distributions. Results of their analysis of 29 independent studies show that child hemoglobin levels increased significantly in response to malaria interventions, having the greatest impact on children between 6 to 35 months of age.

This objective of this study is to investigate the impact of malaria prevalence indicators on the prevalence of serious anemia in children. We hypothesize that children who live in endemic zones of high malaria prevalence run the highest risk of having hemoglobin measures below 8 g/dl. We control for anemia testing during malaria transmission season. Furthermore, we control for several individual-level socio-demographic and health indicators that have shown to be significant in previous studies related to malaria mortality and morbidity (Gemperli *et al*. 2004); we expect these variables to behave similarly in terms of direction and magnitude of effect. An important contribution of this study is that, in addition to exploiting anemia biomarker data in five malaria endemic countries, it adopts a spatial approach to assessing the importance of this indicator relative to the spatial distribution of malaria prevalence.

MATERIALS AND METHODS

Data sources

The primary source of data used in this study is from Demographic and Health Surveys (DHS) in five West African countries since 2000: Benin DHS (2001), Burkina Faso DHS (2003), Cameroon DHS (2004), Ghana DHS (2003) and Mali DHS (2001) (www.measuredhs.com/pubs/). The DHS database is the most comprehensive database on child survival in Africa, coordinated by Macro International (Calverton, Maryland) and sponsored by the US Agency for International Development (www.measuredhs.com). The five DHS countries in this study were selected because they all include malaria-endemic areas. In addition to the standard demographic, health and nutrition data collected in DHS, they contain information on child hemoglobin levels, GPS points of sample clusters, and data from the malaria module. DHS samples are representative at the national level, and most surveys also produce reliable estimates for sub-national administrative units, such as regions or provinces. The countries included in this study have large sample sizes ranging from over 6,000 households to over 13,000 households. Since such large sample sizes are not needed to ensure a high level of precision in anemia levels, children in a sub-sample of one half or one third of households are usually tested (table 1).

Table 1

The second source of data is from the Mapping Malaria Risk in Africa (MARA/ARMA) project (http://www.arma.org.za). The MARA/ARMA project provides a continental database of the spatial distribution of malaria in Africa (MARA/ARMA 1998). These geospatial estimates of malaria prevalence are derived from environmentally determined models of transmission risk (incorporating long-term averages in monthly rainfall and monthly averages of minimum and maximum temperature), and validated by empirical data (e.g., data on parasite ratios (PR) in children, entomological inoculation rates, malaria incidence) where they are available (Kleinschmidt 2001). When the prevalence estimates are mapped, they are a combination of the modeled climatic variables and an interpolation of observed PR which reflect malaria risk during high transmission season. An important assumption built into the MARA/ARMA estimates is that malaria risk is relatively stable over time, which means for this multi-country study we do not make adjustments to align the year of survey and year of malaria prevalence estimate. Malaria seasonality is controlled for insofar as data on the timing and duration in months of the malaria transmission season is incorporated in the analysis.

Data from the Global Rural-Urban Mapping Project were used in determining the distance from a cluster location to the nearest urban area (CIESIN *et al*. 2004). This dataset is a 30" grid representing the extent of urban areas, and incorporates nighttime lights data and populated place locations from a variety of sources. The benefit of using a continuous measure of urban-ness is that it provides additional information on a respondent's community beyond that available with a dichotomous urban-rural residence variable.

DHS sample clusters geocoded at the time of the survey were used to generate estimates of malaria prevalence and distance to urban extent at each cluster location. Because the Burkina Faso, Cameroon, and Ghana DHS surveys included HIV testing with linked results, the GPS cluster locations for these countries have incorporated in them a small geographic error. This slight displacement error of field locations (including in clusters displayed in maps 2 and 3) is to protect respondents' anonymity where HIV tests results could potentially be linked back to a respondent. Points in urban areas are displaced up to 2 km in any direction, and points in rural areas are displaced up to 5 km in any direction.

Spatial data for malaria prevalence, malaria endemicity, start and end of malaria season, and distance to urban extent were matched to DHS sample clusters by overlaying the geocoded clusters on each spatial dataset. The result was a cluster level estimate for each spatial variable which was assigned to each child in the sample. When measuring distance to urban extent, national boundaries were not taken into account. The nearest urban extent to a particular cluster may be in a different country from that cluster, including a country not included in this study. All spatial analyses and maps were generated using ESRI ArcGIS Desktop software (ESRI, Inc. 2005).

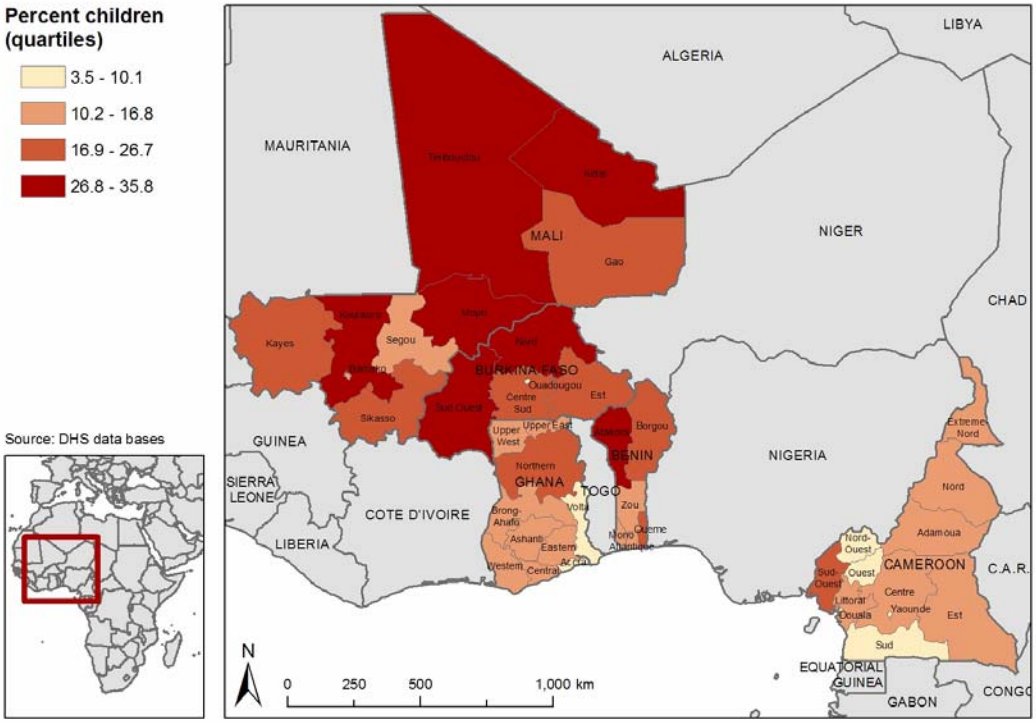
Variable selection & statistical analysis

Logistic regression models were fitted to the distribution of serious anemia in order to estimate the effects of malaria prevalence variables and to identify significant demographic, socioeconomic and health-related explanatory variables. The dichotomous dependent variable, the log odds of children having serious anemia or not, is defined as hemoglobin level less than 8 g/dl. This cut-off has been used frequently as an outcome measure in malaria intervention studies (Korenromp *et al*. 2004). Furthermore, a Hb cut-off at a lower level would have yielded larger standard errors and thus compromised precision. Table 2 shows the prevalence of children 6-59 months with any anemia and with serious anemia, with corresponding relative errors by country. The mean relative error for any anemia (Hb<11 g/dl) is only about 1 percent, and still acceptably low for serious anemia at just under 4 percent.

Table 2

In highly endemic areas, children of younger ages are most vulnerable to malaria, and malaria has the greatest impact on anemia between 6 months and 3 years (Snow *et al*. 1994). By school age, children begin a rapid build-up of immunity (www.malarisite/malaria/children.htm). Our sample comprises children 6 to 59 months, and we control for age groups. Excluded are infants in the first 6 months of life because they are likely to benefit from maternally transferred protection from malaria (Akanmori *et al.* 1995). Map 1 presents the percent of children by sample regions with serious anemia.

Map 1: Children 6-59 months with serious anemia (Hb<8g/dl), by region



Statistical analysis of our sample comprises a series of three logistic regression models where the data for countries is pooled. SAS version 9.1 software (SAS Institute, Inc. 2002-2003) is used for the analysis. The logistic regressions employed to predict the odds that a child is seriously anemic is

$$\text{Logit}(Y_j) \leftarrow \alpha + \beta_k X_{kj}' + \varepsilon,$$

where the 'logit' (Y) is the natural log of the odds that Y=1, or the ratio of probabilities that a child is seriously anemic versus not. α is the intercept, the value of Y when Xs are 0; β_k is a vector of slope parameters representing the change in Y associated with one unit change in X.

Stepwise selection was used to identify significant explanatory variables for serious anemia. Effects were required to meet a significance level of .03 for entry into the model, and a probability level of .05 was required for the variable to stay in the model. Hosmer and Lemeshow's chi square based statistic is used to assess the model's overall goodness of fit. A large *p* value ($p>0.05$) indicates support for the null hypothesis that the data fit the model.

Table 3 shows the percent distributions, by each country in the study, for variables included in the logistic regression models. These variables are grouped into three sets for three multivariate regression models: model one includes malaria prevalence variables; model two combines individual level socio-demographic and health variables; and model three adds the urban extent variable. Country is included in each model as a control variable and Cameroon, with the lowest prevalence of serious anemia, is selected as the reference country. This country control is believed to represent the net effect of unmeasured influences that are not otherwise accounted for in the models.

Table 3

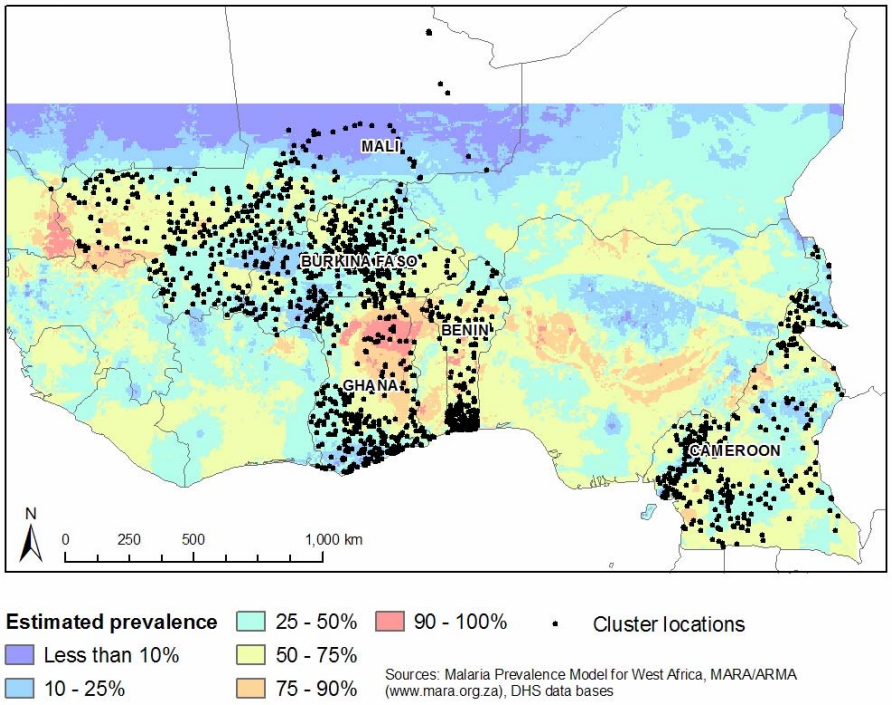
Malaria prevalence variables. Since the main objective of this study is to identify significant malaria risk predictors of serious anemia in children, one of the first tasks was to examine the malariometric data

available to link to the DHS population-based surveys. MARA/ARMA (1998) has created a continental database of malaria survey results in Africa from which have been developed several malaria models using different input data (e.g., Snow 1999b, Kleinschmidt et al 2001, Omumbo et al. 2005). Statistically generated estimates from these models provide the spatial distribution of malaria endemicity, malaria prevalence and the start and end of malaria transmission seasons. These malaria prevalence-related variables, along with months of malaria transmission, have been mapped across Africa in the MARA/ARMA climate suitability maps for endemic malaria (Craig 1999). A summary of these data by country is presented in table 4. The estimates are derived from annual averages of climate and environmental variables, such as rainfall, temperature and altitude, and then categorized into climate suitability categories including: no transmission in an average year, epidemic or strongly seasonal (1-3 months), endemic and seasonal (4-6 months) and endemic and perennial (7-12 months). Elsewhere researchers have classified areas as 'intensely malarious' if the experience transmission for more than 6 months, less than 6 months as moderately malarious, and malaria-free (Omumbo *et al.* 2002). After an exploratory inspection of the MARA/ARMA climate suitability data, we created a dichotomous variable to classify sample clusters as endemic or not endemic. If a cluster is located in an area where malaria transmission occurs during seven to twelve months, then it is considered 'endemic'.

Table 4

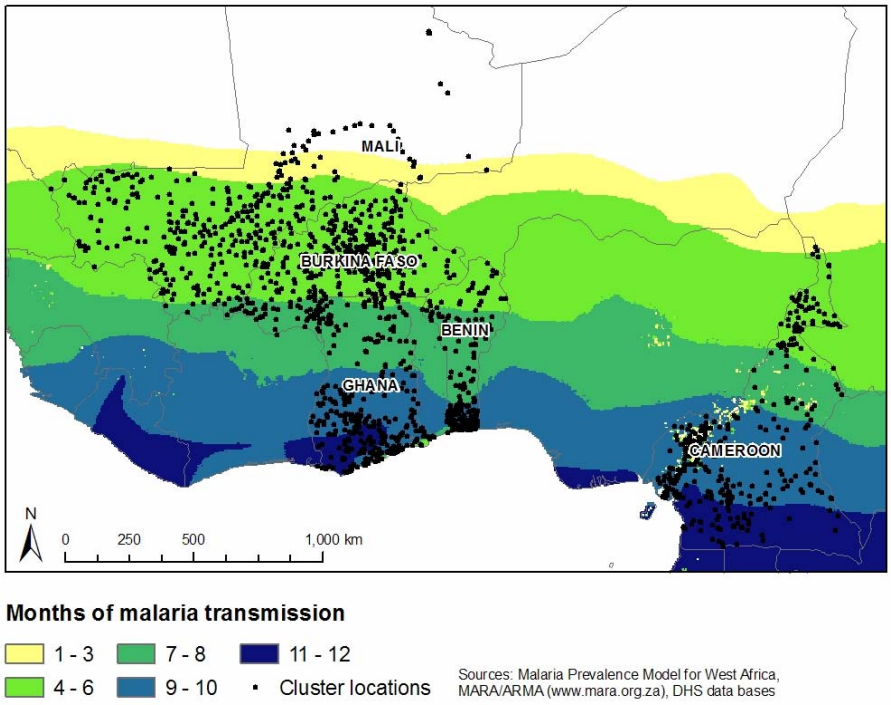
The malaria prevalence estimates used in this study are from malaria distribution maps for West Africa. The spatial statistical models were developed by Kleinschmidt *et al.* (2001) and provide continuous measures of malaria prevalence based on empirical data of parasite ratios in children. Extrapolations to regions with no empirical data available are made using long term averages of climatic and environmental conditions that in other areas were found to be correlated with malaria prevalence. The prevalence measures represent the predicted risk of malaria infection for children under age 10 years during a location's main malaria season. Map 2 shows the distribution of malaria prevalence with sample clusters plotted. Prevalence estimates for sample clusters were pooled and then categorized into risk quartiles for easier interpretation in regression models: high prevalence (57-98%), medium high prevalence (44-56%), medium low prevalence (29-43%), and low (or no) prevalence (0-28%).

Map 2. Estimated malaria prevalence and sample cluster locations



The malaria seasonality maps produced by MARA/ARMA define the start and end boundaries of malaria transmission season. Map 3 shows the distribution of malaria transmission season with sample clusters plotted. This information is used to control for the timing of the interview and anemia testing, i.e., whether they occurred during malaria transmission season or not.

Map 3: Length of malaria transmission season (months) and sample cluster locations



Socio-demographic and health variables. The individual-level independent variables chosen were those found to be significant, or hypothesized to be significant, in previous studies on child mortality and morbidity (Balk et al. 2003, Gemperli et al 2004). These include sex, age, birth order, mother's education and wealth status. In addition, we controlled for nutrition which, like malaria, may be linked to climatic conditions (Nube & Sonneveld 2005), Finally, using data collected from the DHS malaria module testing, we are able to control for whether 'most or all of children' under age five years slept the previous night under a bednet.

Urban extent variable. This is a cluster-level, continuous variable that was categorized into three intervals of distance to reflect urban residence, semi-urban residence, and rural residence.

RESULTS

The relationship between malaria prevalence and hemoglobin levels in children was first investigated by examining their linear association. Table 5 presents the Pearson correlation coefficients for each country by using pairs of these variables for each cluster where children were tested for anemia during malaria transmission season. Although the relationship is not strong across countries, it is a highly significant relationship in the direction hypothesized: a negative association indicating that higher malaria prevalence is associated with lower hemoglobin levels (i.e., anemia). The association is strongest in Burkina Faso ($r= -0.221$) and about the same ($-0.086 < r < -0.064$) in other countries. No coefficient is calculated for Mali since no anemia testing during the Mali DHS survey took place during malaria transmission season.

Table 5

Table 6 presents the odds ratio estimates and confidence intervals for the three multivariate logistic regression models. In these models the data are pooled for the five countries. The data fit the models

increasingly well with each set of variables added. Homer and Lemeshow's goodness of fit statistics for models 2 and 3 have *p*-values large enough that the null hypothesis that the data fit the models is easily accepted; the same statistic for model 1, however, showed that the data were not a good fit. Overall, variables in the final model explain about 13 percent of the total deviance (max-rescaled R-square 0.1308). The greatest improvement in R-square was between model 1 and model 2 (0.046 and 0.1248, respectively), when individual-level control variables were added.

Country is a control variable that remained significant in all three models indicating that all countries had higher levels of serious anemia than Cameroon, the reference category. With additional variables added, however, country effects are attenuated after the first model, and especially for Ghana where in models 2 and 3 the confidence interval includes '1.00' and therefore the direction of risk cannot be determined. Children fare the worst in Mali where they are about three times as likely as children in Cameroon to suffer from serious anemia.

The results for the set of malaria-related variables are not all in the directions hypothesized, but they are not entirely unexpected. Malaria prevalence quartiles remain significant across the models, but the odds of serious anemia for children living in low and medium-high prevalence categories are not distinguishable from the odds of children living in the highest prevalence areas (the 95% confidence intervals include '1.00'). Contrary to the hypothesized direction, children in the medium-high prevalence are actually at higher risk for serious anemia than children in high prevalence areas. Although a negative, linear relationship was hypothesized between anemia and malaria prevalence, plausible explanations for the opposite result is discussed in the next section.

The second malaria-related variable that indicates endemicity (an area with 7+ months of malaria transmission) became significant only in the third model when distance from urban settlement was included. This is evidence that an area's endemicity attribute has a negative impact for children living outside of an urban area (>5 km). The last malaria-related variable is the timing-of-interview variable which remained highly significant across the three models and reveals the importance of gathering hemoglobin measures during malaria season if this is be a proxy for measuring progress in reversing the burden of malaria.

Table 6

Variables in the second model are included as controls for various effects of maternal, socio-demographic and health characteristics. We did not expect child's sex to be a significant determinant for serious anemia. It barely surfaced as a significant variable in model 2, and fell out again in model 3. The direction and magnitude of the effect of child's age are as hypothesized: younger children, after the early months of malaria immunity transmitted from their mother has worn off, have significantly higher odds than older children for having serious anemia. Children in the youngest age group, 6-23 months, not yet having developed adequate immunity, are just beginning to explore their environment independently, and also probably having some of their first encounters with *P falciparum* mosquitoes and, subsequently, malarial anemia. They are almost 4 times more likely than children 42-59 months to have serious anemia. In addition, children in the youngest age group may have a less diverse diet than the older cohorts and thus be more prone to iron-deficient anemia. Strong evidence of the importance of nutritional status is evident in models 2 and 3 that show that children with low weight for their age (less than 2 standard deviations below the international reference median) are about one and a half times more likely than children with normal weight for age to have serious anemia. Mother's education is a control variable that remained highly significant in the expected direction: the less education that a child's mother has, the more likely he or she is to have serious anemia.

Sleeping under a mosquito net did not provide the robust effects we were expecting to see. In model 2, at least, there is evidence that children have smaller odds of serious anemia if 'most or all' children under age 5 years sleep under a net. The lack of more robust results may be a problem with the

operationalization of the variable; this dichotomous variable simply flags those households where most or all of the children slept under a bednet. It does not identify individual children who slept under a net. On the other hand, it may be a problem with not controlling for the type of bednet, i.e. whether it is treated with an insecticide or not. Although the variable in this study does not control for this information, it could (and should) be reconstructed from the DHS malaria module to take into account these nuances. Our proxy for wealth status did not stay in the models and this could also be indicative of a problem with the measure. DHS produces wealth quintiles for countries, but because the index varies slightly in its components across countries it is not recommended that they are compared in a pooled analysis (Rutstein and Johnson 2004). As a proxy for wealth, we used a dummy variable indicating whether or not the household owned a radio and/or a television.

Distance from an urban area is a spatial variable included in the third model. Its effect is significant and reveals that children outside of an urban area are one and a half more times likely to have serious anemia than children living in an urban area.

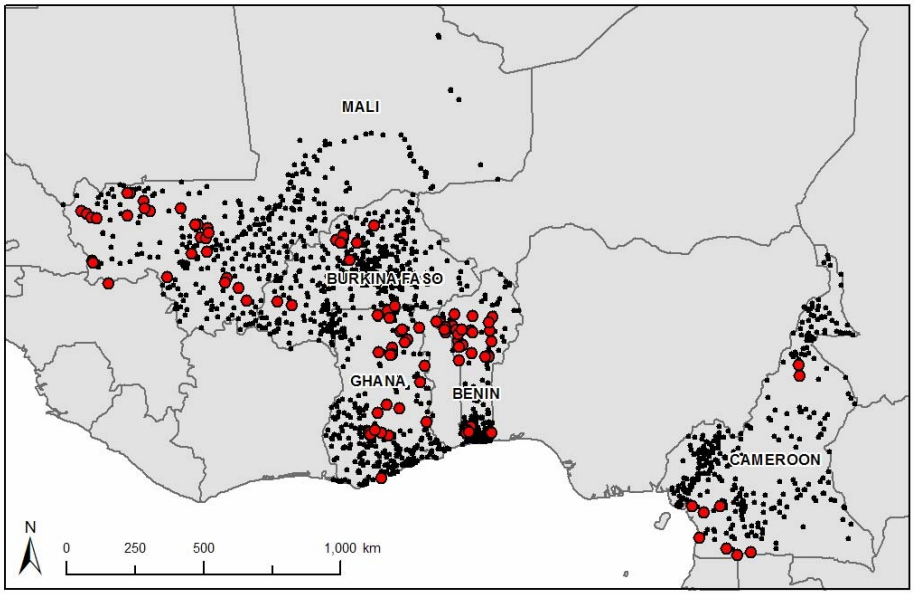
Finally, to summarize the effects of the malaria-related variables, the individual level variables and the urban extent spatial variables (all of the variables in the models), we examine the odds of having serious anemia for a hypothetical child in the 'worst-case scenario' versus one in the 'best-case scenario'. For a child in the 'worst' category of every variable, the odds of having serious anemia are 1.95 (probability 0.66). For another child enjoying the most beneficial category of each variable, the odds of having serious anemia are only 0.11 (probability 0.10). The ratio of these odds best sums up the total potential effect of the explanatory variables on having serious anemia: the likelihood of a child having serious anemia in the worst-case scenario is 17.5 times that of a child in the best-case scenario.

DISCUSSION

The primary objective of this study was to use malaria risk indicators, namely the distribution of malaria prevalence and endemicity, to predict serious anemia in children. Since exposure to acute and chronic malaria episodes in young children leads to serious anemia if left untreated, our hypothesis was that childhood anemia levels would correlate with highly malarious zones. Findings provide information on the utility of using population-based hemoglobin measures as an indicator to monitor malaria morbidity.

The results of the study are mixed. The observed association between malaria and anemia is summarized visually in map 4, which presents the sample clusters where high prevalence of anemia and high prevalence of malaria are identified. Only 6 percent of clusters (106) fall both into the top quartile of percent of children with anemia and in the top quartile of malaria prevalence. Moreover, a case by case examination of children cases in the top decile of predicted probabilities of having serious anemia (phat $\geq$ 0.39) reveals that most of them (62 percent) live in medium-high and medium-low prevalence areas: 20 percent live in high malaria prevalence areas, 30 percent in medium-high prevalence areas, 32 percent in medium-low prevalence areas and 18 percent in low prevalence areas.

Map 4: Clusters with high prevalence of serious anemia in children 6-59 months and located in high malaria prevalence areas.



- Clusters in top quartile of percent with anemia and top malaria prevalence quartile (106)
- Clusters not in both top quartiles and clusters with 2 or fewer cases tested

Sources: Malaria Prevalence Model for West Africa, MARA/ARMA (www.mara.org.za), DHS data bases

These ostensibly paradoxical findings are not the first. Previous studies have also found that the risks of severe malaria disease in childhood are low in areas of low transmission intensity, and also low in areas of highest transmission intensity; conversely, malaria morbidity is highest under low-to-moderate transmission intensities (Marsh *et al*. 1999, Snow *et al*. 1997). There are several plausible explanations for these findings, and they are not mutually exclusive from each other. All of them are open to further discussion and to further research.

The first set of explanations has an epidemiological foundation. In highly endemic areas, young infants have a high exposure to malaria infection and thus develop immunity more rapidly than children in less intense transmission areas. Immunity to malaria also implies protection against malaria-induced anemia. The 'nuisance factor' may also be in effect where mosquitoes are more prevalent; those who can afford bednets, insecticide and other preventive mechanism will use them to stay comfortable and, consequently, disease-free. The health system may avail curative measures and prophylaxis more readily to a population in areas of high transmission. In contrast, in medium-high prevalence areas the malaria transmission season may be less predictable and hence fewer preventive and curative measures remain in place to combat the disease.

The second set of explanations makes explicit potential weaknesses in the model and data. Outside of controlling for children below age five sleeping under mosquito nets the previous night, the models do not account specifically for insecticide treated nets, nor for other preventive measures such as prompt and effective treatment, insecticide spraying campaigns and prevention and control of malaria in pregnant women (although this may be independent of children in our study who are at least 6 months of age). The burden of malaria in high prevalence areas may also be underestimated because young infants who are the most vulnerable to malaria disease are most likely to die of the disease within the first two years of life; the older children, therefore, represents the most resistant, healthy members of their cohort.

The third set of explanations concerns the accuracy of malaria prevalence data for our sample clusters. The model estimates in the continental data set of malaria risk are continuously being refined as more empirical data on parasite ratios, incidence of malaria, etc. become available. In the West Africa models we used there were several regions for which empirical data were not available (poorly covered by parasite ratio or malaria incidence surveys) and thus the predictions are entirely based on statistical models. Ghana, for example, had a sparse coverage of empirical data points and hence the predictions were model dependent rather than interpolation driven (Kleinschmidt 2001). Even with the best refinements, however, the model estimates are based on long term climatic averages that vary to some extent annually. This will affect malaria transmission, especially in low and moderate transmission areas that are more prone to epidemics. These extraordinary seasons are difficult to predict accurately, and perhaps impossible to predict on a continental scale.

CONCLUSION

Despite some of the epidemiological complexities and shortcomings in the model, we maintain that childhood anemia levels hold important value as one strategy to monitor malaria burden. Physiologically, anemia is almost inevitably the outcome in young children suffering from acute or chronic malaria, and especially for those under age 6-23 months. Furthermore, population-based Hb measures are highly reliable. They are data with measurably high levels of precision, sensitive to detecting changes attributable to interventions. In this study, the standard error was within 4 percent of the mean in every sample country (SE ranging from 0.029 and 0.036 corresponding to means of 8.83 and 10.10).

The validity of Hb measures, that is, how well does this indicator actually measure malaria morbidity, depends on whether or not anemia testing is done during malaria transmission season. This study provides clear evidence that children tested for anemia during the malaria transmission season were at higher risk of anemia than those not tested during the malaria season. The validity of the measure as an indicator for malaria burden is limited insofar as the cause of anemia is multifactorial. In areas endemic to malaria it is likely to be the main factor, or at least an important contributing factor, to anemia. In areas outside of stable transmission it may be worth exploring the feasibility of coupling hemoglobin measures with rapid diagnostic tests, appropriate to use in the field, to confirm the presence of malaria infection.

Finally, this study demonstrates the value of combining spatial and non-spatial data in assessing indicators for population health. Variables derived from spatial datasets were combined with survey databases in constructing the variables used in this analysis. The malaria-related variables were essential to the analysis, while the information on a child's distance to an urban area provided additional valuable information on the potential burden of malaria in that child's community. Map 4 demonstrates a possible technique useful for pinpointing areas in particular need of interventions. The potential benefits of mapping areas with particularly high malaria burdens are great, and this paper provides only a limited example of the importance of spatial analytic techniques in this area.

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Table 1. Description of samples from five DHS countries in West Africa

	Burkina Faso 2003	Benin 2001	Cameroon 2004	Ghana 2003	Mali 2001
Number of clusters	400	247	466	412	402
Number of households	9470	6206	11556	6628	13717
Household subsample for anemia testing	1/3 HH	1/2 HH	1/2 HH	All HH	1/3 HH
Number of children age 6-59 months tested for anemia	2817	2300	3575	3016	2843

Source : DHS databases (www.measuredhs.com/)

Table 2. Anemia prevalence estimates for sample clusters, five DHS countries in West Africa

	Burkina Faso 2003	Benin 2001	Cameroon 2004	Ghana 2003	Mali 2001
Percent of children 6-59 months with:					
Any anemia (Hb<11.0 g/dl)	91.5	81.9	67.3	76.0	82.8
(Relative SE, percent)	(0.55)	(0.98)	(1.18)	(0.91)	(0.84)
Serious anemia (Hb <8 g/dl)	27.6	20.0	11.2	14.2	24.8
(Relative SE, percent)	(2.90)	(4.00)	(4.46)	(4.23)	(3.24)
Number of children age 6-59 months tested for anemia	2817	2300	3575	3016	2843

Source : DHS databases (www.measuredhs.com/)

Table 3. Percent distributions of children 6-59 months, DHS and MARA/ARMA data from five countries in West Africa

	Burkina Faso 2003	Benin 2001	Cameroon 2004	Ghana 2003	Mali 2001
Malaria prevalence (quartiles)					
Low	14.2	13.2	23.1	22.2	30.6
Medium-low	36.8	19.3	18.3	19.6	23.6
Medium-high	32.8	15.6	36.4	14.2	23.9
High	16.2	51.9	22.2	44.0	21.9
Anemia testing during malaria season					
No	13.3	12.1	43.5	5.4	100.0
Yes	86.8	87.9	56.5	94.6	0.0
Endemic zone					
No	93.1	12.1	42.3	7.9	98.1
Yes	6.9	87.9	57.7	92.1	1.9
Sex of child					
Girl	48.9	49.7	49.3	50.6	48.7
Boy	51.1	50.3	50.7	49.4	51.3
Age group (months)					
6-23	34.9	33.8	35.6	33.6	33.7
24-41	34.3	33.3	31.8	34.3	34.0
42-59	30.9	32.9	32.6	32.1	32.2
First born					
No	81.5	79.7	78.1	78.7	86.1
Yes	18.5	20.3	21.9	21.3	13.9
Mother's education					
No formal education	89.5	74.6	30.1	39.2	84.3
Primary	7.9	18.8	43.5	23.2	11.5
Secondary or higher	2.6	6.6	26.4	37.6	4.3
Nutritional status					
Normal	79.8	91.9	92.8	89.4	84.6
Low weight for age	20.2	8.1	7.2	10.7	15.4
Slept under mosquito net					
No children <5 slept under net/No net	76.2	63.7	85.9	84.0	57.2
Most or all children < 5 slept under net	23.8	36.3	14.1	16.0	42.8

Wealth status (quintiles)					
First (lowest)	17.7	24.6	24.2	25.8	25.5
Second	22.4	21.1	22.4	22.1	20.6
Third	27.2	19.9	22.1	19.9	19.3
Fourth	18.1	20.4	17.2	17.5	18.9
Fifth (highest)	14.6	14.0	14.2	14.8	15.7
Distance from urban area					
< 5 km	26.6	39.8	42.9	39.1	27.7
5-25 km	48.3	47.8	37.2	47.8	30.3
> 25 km	25.1	12.4	19.9	13.1	42.1
Number of children	2817	2300	3575	3016	2843

Source : Malaria Prevalence Model for West Africa, MARA/ARMA (www.mara.org); DHS databases (www.measuredhs.com/)

Table 4. Length of malaria transmission season and malaria prevalence estimates, MARA/ARMA data from five countries in West Africa

	Burkina Faso 2003	Benin 2001	Cameroon 2004	Ghana 2003	Mali 2001
Length of transmission season (months)					
Range	3-7	5-9	1-12	5-12	0-7
Average	5.4	8.1	7.7	9.1	4.9
Median	6	9	9	9	5
Malaria prevalence					
Range	0.10-0.68	0.13-0.89	0.07-0.90	0.04-0.95	0.0-0.87
Average	0.43	0.52	0.45	0.52	0.41
Standard deviation	0.13	0.18	0.16	0.23	0.18
Median	0.44	0.59	0.48	0.52	0.42

Source : Malaria Prevalence Model for West Africa, MARA/ARMA (www.mara.org)

Table 5. Pearson correlation coefficients for level of Hb (g/dl) in children age 6-59 months and malaria prevalence level in clusters in which they live, for clusters where anemia was measured in malaria endemic clusters during malaria transmission season, DHS and MARA/ARMA data

	Burkina Faso 2003	Benin 2001	Cameroon 2004	Ghana 2003	Mali 2001
Correlation coefficient	-0.221	-0.086	-0.073	-0.064	na
Significance level	<.0001	0.0001	0.0013	0.0007	na
Number of pairs	345	2010	1923	2815	na

na = no children were tested for anemia during high malaria transmission season

Source : Malaria Prevalence Model for West Africa, MARA/ARMA (www.mara.org); DHS databases (www.measuredhs.com/)

Table 6. Odds Ratio estimates and confidence intervals for serious anemia (Hb < 8g/dl), children 6-59 months, DHS and MARA/ARMA databases

	Model 1		Model 2		Model 3	
	OR	95% C.I.*	OR	95% C.I.*	OR	95% C.I.*
Country	<.0001		<.0001		<.0001	
Burkina Faso	2.59	2.26, 2.97	1.99	1.68, 2.37	2.25	1.85, 2.73
Benin	1.68	1.44, 1.97	1.42	1.18, 1.71	1.44	1.20, 1.74
Cameroon (Ref)	1.00		1.00		1.00	
Ghana	1.20	1.03, 1.40	1.14	(0.96 1.36)	1.10	(0.92, 1.31)
Mali	3.81	3.17, 4.59	3.13	2.52, 3.88	3.10	2.49, 3.88
Malaria-related variables						
Malaria prevalence (quartiles)	<.0001		0.0029		0.0246	
Low (0.00-0.28)	0.91	(0.81, 1.03)	0.96	(0.84, 1.11)	0.99	(0.86, 1.14)
Medium-low (0.29-0.43)	1.06	(0.94, 1.19)	1.12	(0.99, 1.28)	1.11	(0.98, 1.27)
Medium-high (0.44-0.56)	1.14	1.02, 1.29	1.21	1.06, 1.38	1.19	1.04, 1.36
High (Ref) (0.57-0.98)	1.00		1.00		1.00	
Endemic zone (7+ months of malaria transmission)	Excl.		Excl.		0.0308	
Yes					1.18	1.02, 1.37
No (Ref)					1.00	
Anemia testing during malaria season	0.0044		<.0001		<.0001	
Yes	1.66	1.39, 1.98	1.72	1.42, 2.09	1.55	1.26, 1.90
No (Ref)	1.00		1.00		1.00	
Individual-related maternal, socio-economic and health variables						
Sex of child			0.0482		Excl.	
Boy			1.10	1.00, 1.20		
Girl (Ref)			1.00			
Age group (months)			<.0001		<.0001	
6-23			3.87	3.41, 4.40	3.90	3.43, 4.42
24-41			1.87	1.64, 2.14	1.87	1.64, 2.14
42-59 (Ref)			1.00		1.00	
First born			Excl.		Excl.	
Yes						
No						
Mother's education			<.0001		<.0001	
No formal education			1.79	1.52, 2.11	1.57	1.33, 1.87
Primary			1.31	1.10, 1.57	1.21	1.01, 1.46
Secondary or higher (Ref)			1.00		1.00	
Nutritional status			<.0001		<.0001	
Low weight for age			1.44	1.27, 1.63	1.43	1.26, 1.62
Normal (Ref)			1.00		1.00	
Slept under mosquito net			0.0297		Excl.	

Table 6. Odds Ratio estimates and confidence intervals for serious anemia (Hb < 8g/dl), children 6-59 months, DHS and MARA/ARMA databases

Most or all children < 5 years slept under net		0.89	0.79, 0.99			
No children slept under net/No net		1.00				
Wealth status (has radio and/or TV)		Excl.		Excl.		
Yes						
No						
Spatial variable						
Distance from urban area				<.0001		
< 5 km (Ref)				1.00		
5-25 km				1.51	1.32, 1.73	
> 25 km				1.52	1.35, 1.70	
Intercept (Constant)	-1.5417	1.69950		-1.63781		
Number of cases	14666	12331		12331		
Df	8	15		16		
-2 Log Likelihood	14441.3	123570		12357.0		
Max-rescaled R-Square	0.0460	0.1248		0.1308		

*Wald confidence intervals for adjusted odds ratios

( ) indicates odds ratio confidence interval for which the estimate includes 1.00, and therefore not a substantial difference in risk compared to the reference category.

'Excl.' indicates that a variable was not selected for the model in the stepwise regression procedure