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BRIEF REPORT

The Burden of Malaria in the Democratic Republic of the Congo

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Despite evidence that older children and adolescents bear the highest burden of malaria, large malaria surveys focus on younger children. We used polymerase chain reaction data from the 2013–2014 Demographic and Health Survey in the Democratic Republic of Congo (including children aged <5 years and adults aged ≥15 years) and a longitudinal study in Kinshasa Province (participants aged 6 months to 98 years) to estimate malaria prevalence across age strata. We fit linear models and estimated prevalences for each age category; adolescents aged 10–14 years had the highest prevalence. We estimate approximately 26 million polymerase chain reaction–detectable infections nationally. Adolescents and older children should be included in surveillance studies.

Keywords. malaria; Democratic Republic of the Congo; adolescents; *Plasmodium falciparum*.

Growing evidence suggests that malaria cases are concentrated among older children and adolescents 5–14 years old, a group often excluded from national malaria studies. Recent studies from across sub-Saharan Africa found that the prevalence of malaria in children and adolescents >5 years old was higher than among children aged ≤5 years [1–3]. However, large malaria surveys and databases do not specifically estimate prevalence among adolescents. The Malaria Indicator Surveys focus on children <5 years old. The Malaria Atlas Project (MAP) and the World Health Organization estimate the total number of cases and incidence rates across all age categories but do not present age-specific estimates [4, 5]. Although these sources supply critical information, national malaria control programs need robust data across age strata to inform policy making. This is particularly true in the Democratic Republic of the Congo (DRC), where 12% of the world's malaria cases occur but the national prevalence among children aged 5–14 years is unknown [5].

To estimate the burden of infection in the DRC across age strata, we used data from the Demographic and Health Survey (DHS) conducted in 2013–2014 and an ongoing longitudinal study. The former included >8000 children aged <5 years and >17 000 adults aged ≥15 years, and the latter included 1591 people at 7 sites in Kinshasa Province with varying endemicity. These combined data sources enabled us to interpolate malaria prevalence across all age strata and produce national prevalence estimates that can be used to target interventions more effectively.

METHODS

Longitudinal Study Population

A longitudinal study of malaria has been conducted at 7 sites in Kinshasa Province since 2015, as described elsewhere by Mwandagalirwa et al [6]. Briefly, from February to May 2015, households were randomly selected from the 7 sites, and household members were asked to participate. In total, 1591 participants, aged 6 months to 98 years, were enrolled from 6 rural villages and 1 urban neighborhood in Kinshasa.

Dried blood spot samples were collected from each participant, and DNA was extracted using Chelex resin and saponin, as described elsewhere [7]. Polymerase chain reaction (PCR) targeting the *Plasmodium falciparum* lactate dehydrogenase gene was performed on all samples. Full details regarding the PCR methods are available in elsewhere [6]. PCR data were available for 1557 participants at enrollment. Village-level malaria prevalence ranged from 3% in the urban site to 42% in one of the rural villages.

DHS Population

The DHS Program conducts nationally representative population-based surveys using a random sampling scheme [8]. The most recent DHS in the DRC was conducted between November 2013 and March 2014. Informed consent was obtained from each participant, or a parent/guardian for individuals <18 years old [8]. In addition to completing the standard DHS questionnaire, dried blood spot samples were collected from each participant and sent to the University of North Carolina for malaria molecular testing [9].

Because malaria epidemiology differs between rural and urban areas, we divided the DHS data into urban and rural

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clusters before modeling [7]. Owing to the risk of misclassification of urbanicity in large surveys with complex sampling frames, we used a previously established principal component analysis (PCA) method to assign each subject's urban or rural status (see Supplementary Text) [9, 10]. As a sensitivity analysis, we also conducted the analysis using the DHS urban/rural classifications to determine whether there were substantial differences between methods. The correlation between the PCA-derived and the DHS urban/rural categories is 0.75 [9].

Modeling

We estimated prevalence for the missing 5–9- and 10–14-year-old age categories in the DHS by fitting a linear model with DHS prevalence as the outcome and age category and prevalence from the longitudinal study as covariates. We modeled the urban and rural DHS clusters separately and used 2 modeling strategies to estimate a range of prevalence estimates and PCR-detectable infections. Both strategies used data from the rural longitudinal villages to interpolate prevalence estimates for the rural DHS clusters. However, for the first modeling strategy (model 1), we used data from the longitudinal study's urban site to interpolate prevalence estimates for the urban DHS clusters. This model assumed that data from the urban longitudinal site are representative of the urban DHS clusters.

For the second modeling strategy (model 2), we used data from the longitudinal study's rural sites to interpolate prevalence estimates for the urban DHS clusters. This assumed that the rural villages from the longitudinal study are representative of the urban DHS clusters. We then used the model estimates to interpolate prevalence estimates for the 2 missing age categories from the DHS data. We used model 2, because the urban sites from the longitudinal study may not be representative of the urban DHS sites (urban sites within the mega-city of Kinshasa may not reflect urban sites in other regions of the DRC). Rather, the rural longitudinal study sites may be more representative of the urban DHS sites. Using both modeling strategies provided a range of prevalence estimates.

We determined the variance of the prevalence estimates using nonparametric bootstrapping. We resampled individuals with replacement in the both longitudinal study and DHS study to re-run the models 1000 times and generate 1000 prevalence estimates for each age category. We estimated the standard error as the standard deviation of the 1000 estimates and used this to generate 95% confidence intervals for each estimate. We did this separately for models 1 and 2. To compare our prevalence estimates with parasite rate estimates from MAP, we also modeled PCR prevalence for children aged 2–10 years specifically, using the same modeling techniques described above.

WorldPop Population Estimates

To estimate the total burden of malaria in the DRC, we used age-specific population data for the DRC developed by the WorldPop Project [11]. Province boundaries were retrieved from the Humanitarian Data Exchange database and used to derive province-specific population totals from the 2015 WorldPop age-specific population grids [12]. The population for each 5-year age category was calculated for each DRC province using the zonal statistics function in ArcGIS software (version 10.5.1; Esri).

The proportion of residents living in urban areas was determined for each province using the cluster urban/rural classifications. Because the sampling clusters are representative of the population for each province (when sampling weights are applied), the proportion of DHS participants in urban clusters represents the proportion of residents living in urban areas within the province. We then generated the total number of urban and rural dwellers in each age category for each province. We applied the modeling results to the population estimates to estimate the total number of malaria cases in the DRC.

RESULTS

Longitudinal and DHS Studies

PCR data were available for 1557 individuals in the longitudinal study and 25 105 from the DHS. Characteristics of both populations are presented in Supplementary Table 1.

The plot of malaria prevalence by age category demonstrates that the highest prevalence of malaria in the longitudinal cohort is among 10–14-year-old children in rural villages, followed by 5–9-year-old children (Figure 1A and Supplementary Table 2), as has been reported elsewhere [6]. In the urban site, prevalence remains relatively similar across age categories. The DHS data indicate that malaria prevalence in both urban and rural areas is more similar to that of the rural villages in the longitudinal study than the urban site.

Modeling

Modeling results indicate that the prevalence of infection among adolescents approaches 50% in rural areas. In urban areas, model 1 predicts prevalences of approximately 24.5% among children aged 5–9 and 24.3% among those aged 10–14 years (Figure 1B and Supplementary Table 3). Model 2 predicts prevalences of 32.4% and 33.8% among children aged 5–9 or 10–14 years, respectively (Figure 1C and Supplementary Table 3). The sensitivity analysis confirmed that estimates from models using the DHS urban/rural categories were similar to those generated using the PCA urban/rural classifications (Supplementary Figure 1 and Supplementary Table 4). The estimated prevalence for children aged 2–10 years, weighted by the proportions of children in urban and rural areas, were 36.2% (model 1) and 38.5% (model 2).

Burden Estimates

Applying the modeling results to the WorldPop data, we estimate that the total number of infections among 5–14-year-olds

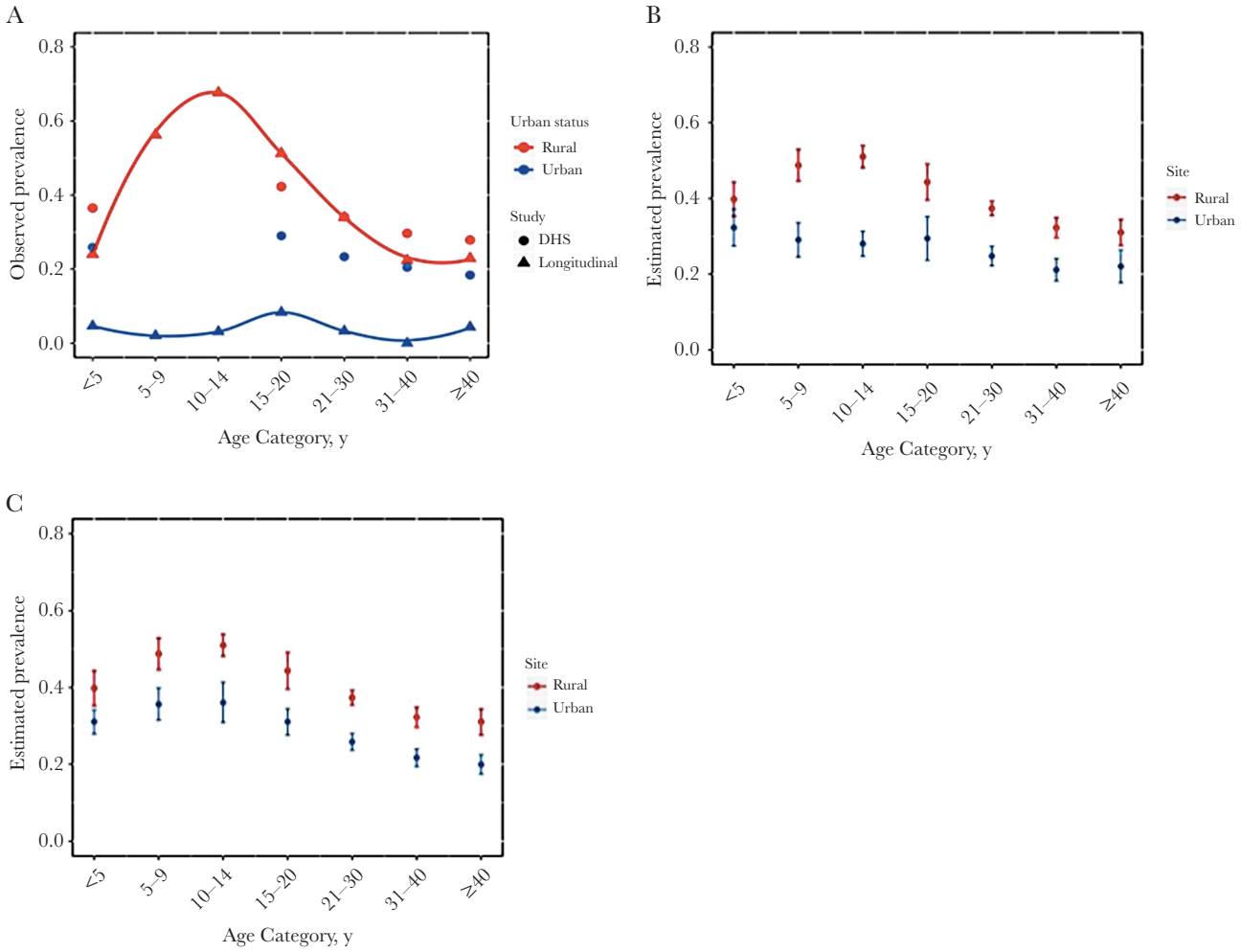

Figure 1. A, Observed malaria prevalence by age in the Democratic Republic of Congo, from the Demographic and Health Survey (DHS), conducted in 2013–2014, and an ongoing longitudinal study; DHS data are shown by urban or rural status. *B, C,* Estimated malaria estimates by age, and by urban or rural sites, according to model 1 (*B*) and model 2 (*C*). (See Modeling for details explanation of models.)

is approximately 10–10.5 million (model 1 estimate, 9 959 468 [95% confidence interval, 8 996 159–10 922 776]; model 2 estimate, 10 572 583 [9 554 776–11 590 390]; Table 1) and an overall burden of approximately 26.2–26.8 million infections (model 1 estimate, 26 235 102 [23 099 342–9 370 862]; model 2 estimate, 26 794 707 [23 829 508–29 759 906]). The estimated

Table 1. Estimated Population and Number *of Plasmodium falciparum* Cases by Age Category in the Democratic Republic of the Congo

			Estimated No. of Infections (95% CI)[a]	
Age Category, y	No. Living in Urban Areas	No. Living in Rural Areas	Model 1	Model 2
<5	4 445 852	10 890 243	5 194 424 (4 454 239–5 934 608)	5 129 856 (4 463 098–5 796 615)
5–9	3 796 128	9 383 888	5 296 336 (4 700 926–5 891 746)	5 593 511 (5 009 408–6 177 615)
10–14	3 321 592	7 836 080	4 663 132 (4 295 233–5 031 030)	4 979 072 (4 545 368–5 412 775)
15–19	2 202 165	4 703 663	2 574 917 (2 177 043–2 972 792)	2 614 046 (2 266 874–2 961 217)
20–29	3 633 689	7 356 944	3 361 155 (3 079 203–3 643 108)	3 408 109 (3 141 321- 3 674 898)
30–39	2 396 450	5 118 434	1 950 005 (1 727 643–2 172 366)	1 969 152 (1 763 075–2 175 229)
≥40	3 938 371	8 453 466	3 195 13 (2 665 055–3 725 212)	3 100 961 (2 640 364–3 561 558)
Total	**23 694 227**	**53 742 718**	**26 235 102 (23 099 342–29 370 862)**	**26 794 707 (23 829 508–29 759 906)**

Abbreviation: CI, confidence interval

[a]Calculated as the estimated number of infections based on the lower and upper bounds of the 95% CI for both rural and urban estimates added together.

age-standardized prevalence from model 1 is 33.8% and 34.6% from model 2. Although the estimated prevalences for children aged 5–9 and adolescents aged 10–14 years differ between models 1 and 2 (7.9% and 9.5%, respectively), the relatively low number of 5–14-year-olds living in urban areas results in overall similar burden estimates for the models (a difference of approximately 600 000 infections).

DISCUSSION

We used data from a longitudinal study in Kinshasa Province and nationally representative DHS data to estimate the national prevalence and burden of infections for children and adolescents aged 5–14 years in the DRC, a group not included in recent national, population-based malaria surveys. To our knowledge, this is the first study to estimate national malaria prevalence proportions specifically for this age group in the DRC. These findings highlight the need to include 5–14-year-olds in national malaria surveys and have important implications for control programs. The DRC may benefit from interventions targeting this age group, such as school-based programs. Programs that focus exclusively on children <5 years old will miss most infected children in the DRC. In addition, these findings have implications for future malaria modeling studies in the DRC, as incorporating an accurate age distribution is critical for properly modeling malaria transmission.

We estimated a high prevalence of infection among older children and adolescents. In rural areas, the highest estimated prevalence of malaria is among 5–14-year-olds, with estimates reaching nearly 50%. In urban areas, the burden of malaria for 5–14-year-olds is as high as, or even higher than, that of children <5 years old. This support previous findings that older children and adolescents in sub-Saharan Africa often bear the highest burden of malaria [1–3, 13]. Thus, the DHS and Malaria Indicator Surveys excluded the most affected population and likely underestimate the true burden of infection.

Because our study focuses on subjects enrolled in cross-sectional household surveys and PCR-detectable infections, we cannot directly compare our overall infection prevalence estimates with World Health Organization and MAP estimates of malaria incidence. However, our 36%–38% prevalence estimate for the 2–10-year-old age stratum was higher than the MAP's 27% estimate from the same time period. This difference could be due to our reliance on a more sensitive assay—we used PCR results, while MAP used primarily RDT data—and/or differences in our modeling approaches.

Our study is strengthened by using data from the largest and most recent nationally representative health survey conducted in the DRC, which included >25 000 children aged <5 years and adults aged ≥15 years. However, the study also has several limitations. First, it relies on prevalence data obtained from subjects at 7 sites in Kinshasa Province, collected during a 3-month period. The DRC is large and diverse, with varying malaria prevalence, and it is possible that these sites are not representative of the DRC. Second, it was limited by poor census data. The most recent population census of the DRC was conducted in 1984, which forced us to rely on external population estimates [14].

As a third limitation, determining urbanicity is complex, and using a binary determination may introduce bias. For example, the rural sites in our longitudinal study are located within Kinshasa Province, which is classified as entirely urban by the DHS. Finally, our models do not incorporate spatial dependence of malaria infection data [4]. Although these limitations mean that the estimates presented here are a crude assessment of the range of malaria prevalence in the DRC, the modeling results remain useful in the absence of comprehensive national studies. Our estimates illustrate the need to study malaria among adolescents and include them in future surveys.

In conclusion, 5–14-year-olds account for a large proportion of malaria infections in the DRC. Future studies that attempt to assess malaria burden in highly endemic countries like the DRC need to include this age stratum.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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