Study population

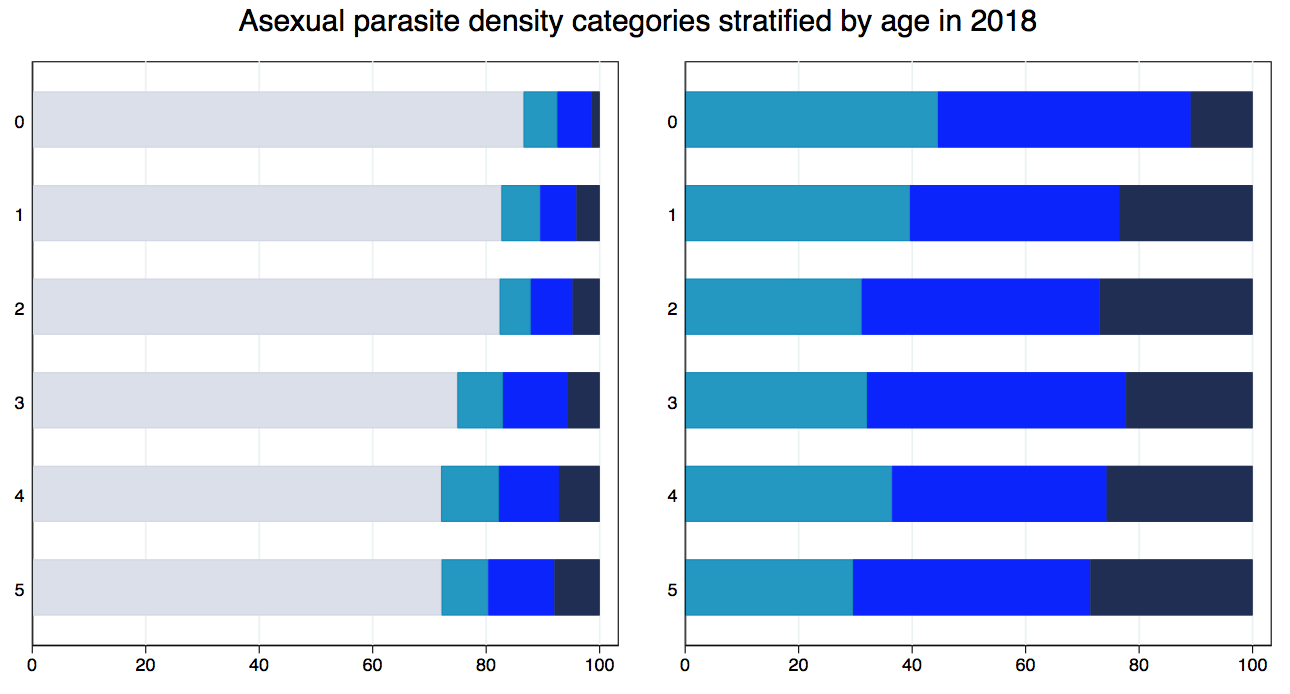
A total of 7783 Nigerian children under 5 years of age participated in the study. Overall, the mean age was 2.4 years (SD = 1.4) and 49.0% were females (3812/7783). Basic study characteristics are presented in Table 1.

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| Table 2: Study population characteristics | | | |
|  | **2018**  (N=7,783) \* |  |  |
| **Age (years), % (n)** |  |  |  |
| 0 | 9.7 (754) |  |  |
| 1 | 21.0 (1,637) |  |  |
| 2 | 21.0 (1,638) |  |  |
| 3 | 22.5 (1,752) |  |  |
| 4 | 21.2 (1,653) |  |  |
| 5 | 4.5 (349) |  |  |
| **Gender, % (n)** |  |  |  |
| Female | 49.0 (3,812) |  |  |
| **Geopolitical zone, % (n)** |  |  |  |
| North-Central | 17.6 (1,368) |  |  |
| North-East | 17.9 (1,391) |  |  |
| North-West | 23.1 (1,797) |  |  |
| South-East | 15.5 (1,207) |  |  |
| South-South | 10.9 (852) |  |  |
| South-West | 15.0 (1,168) |  |  |
| \* N = denominator | | | |

Asexual parasite prevalence was 21.5% (1675/7783) and the asexual parasite densities ranged from 15 to 485,609 parasites/μL, with the geometric mean being 2242 parasites/μL (95% CI = 2032-2473 parasites/μL). Asexual parasite densities did not differ in relation to sex (geometric mean: 2187 parasites/μL, 95% CI: 1909-2505 parasites/μL for males and 2304 parasites/μL, 95% CI: 1998-2657 parasites/μL for females, p-value=0.5).

When including all children in the analysis (those positive or negative for parasites), the proportion with ≥ 10,000 parasites/μL increased with increasing age, with 1.6% in children under 1 years, 4.2% in 1-year olds, 4.8% in 2-year olds, 5.8% in 3-year olds, 7.3% in 4-year olds and 8.0% in 5-year olds (**Figure 4a**). Conversely, the proportion with no infection detected by microscopy decreased with increasing age, with 86.7% in 0-year olds, 82.6% in 1-year olds, 82.3% in 2-year olds, 74.8% in 3-year olds, 72.1% in 4-year olds, 71.9% in 5-year olds (**Figure 4a**). There was strong evidence for a difference between asexual category and age (p<0.001).

When only infected children were included in the analysis, a different pattern emerged (**Figure 4b**). The percentage with ≥ 10,000 parasites/μL was similar in all age groups (between 23.1-28.6%) apart from the in the youngest age group (12.0%). A significant difference between asexual category and age was found (p=0.02), however, this was less significant than when all individuals were included in the analysis.



**Percent (%)**

**Age (years)**

**A**

**B**

Chart

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**Figure 4: Asexual parasite density categories stratified by age in 2018,** highlighting that different information can be understood from analysis based on only positive individuals (B) as compared to when all individuals are included in the analysis (A).

When analysing the geometric mean density by age, a consistent finding to the categorical analysis above was observed, where the youngest age group had the lowest geometric mean (1414 parasites/μL, 95% CI: 985-2030 parasites/μL)(Figure 5). It then increased to a maximum of 2750 parasites/μL (95%CI: 2161-3499) at 2 years of age. After 2 years of age, the asexual parasite density decreased and then increased slightly. There was evidence for a difference between asexual parasite density between age groups (p=0.04). Through conducting pairwise comparisons, this difference was shown to be driven through the 0-year age group being significantly different to the rest (Appendix 1).

Geopolitical zone asexual density differences were investigated on the premise of the zones containing differences in the prevalence of malaria, with the north generally being higher than the south (21). Regarding the distribution of parasitaemia by geopolitical zone in 2018, the highest density was recorded in the North-West (geometric mean 2650 parasites/μL; 95% CI: 2229-3151 parasites/μL) and the lowest in the South-West (geometric mean 1663 parasites/μL; 95% CI: 1296-2133 parasites/μL)(Figure 6). In general, the North had a higher geometric mean asexual parasite density than the South. The 95% CIs for all regions overlapped, however, there was strong evidence for a difference between the asexual parasite density between geopolitical zones (p<0.001). Pairwise comparisons showed that this difference was mainly driven by the North-West and North-Central being significantly different to the Southern geopolitical zones (Appendix 1). Therefore, as a whole the parasite density follows a similar pattern to the parasite prevalence.

Chart

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Although there was a trend of higher densities in the Northern zones of the country, there were also variations in the densities seen within states in each zone (Figure 7).

Map

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**Figure 7: Geographical heterogeneity in asexual malaria parasite density in children under 5 years in Nigeria in 2018**. Geometric mean parasite density was analysed for all 36 states. Names of individual states can be found in Figure 2 and all numbers are provided in Appendix 5.

The results from the geopolitical zone density analysis fit broadly with the previously found malaria prevalence. Therefore, further analysis was conducted to understand if this association between the prevalence and density also occurred in the individual states.The geometric mean asexual parasite density was compared to the asexual parasite prevalence in each state in 2018, finding a moderate positive significant correlation (Spearman’s r=, p=). Therefore, states that had a higher prevalence generally tended to have a higher asexual parasite density (Figure 8).

ADD IN THE CORRELATION GRAPH – NEED TO WORK OUT HOW TO PRODUCE 95% CI OF PROPORTION

**Figure 8: Scatterplot showing a moderate positive significant correlation between asexual prevalence and density for each state in 2018.** Lines indicate the 95% CI for the density and prevalence for each state. The point to the very left of the graph corresponds to Lagos and it does not contain a 95% CI for asexual density because the upper limit was 524,280 parasites/μL. All numbers are provided in Appendix 5.

### Sexual parasite prevalence and density

Overall sexual parasite prevalence was 7.8% (604/7783) and children under 1 year had the lowest prevalence of sexual parasite (4.9%, 95% CI: %) and children aged 4 years had the highest prevalence (9.7%, 95% CI: %)(Table 3). The sexual prevalence increased with increasing age, except in the oldest age group where it decreased again. The sexual prevalence followed a very similar pattern to the asexual prevalence: it was higher in the northern zones than in the southern (Table 3).

Looking at the association between asexual and sexual prevalence in each state, a strong positive significant correlation was found (Spearman’s r=, p<)(Figure 9). Therefore, states with a higher asexual prevalence tended to have a higher sexual prevalence.

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| Table 3: Sexual parasite prevalence according to sex, age and geopolitical zone in 2018 | | | |
|  | **Sexual parasite prevalence, % (n)**  **(N=7783)** | **95% CI (%)** | **p-value\*** |
| **Sex** |  |  |  |
| Male | 8.2 (324/3647) |  |  |
| Female | 7.3 (280/3532) |  | 0.20\* |
| **Age (years)** |  |  |  |
| 0 | 4.9 (37/717) |  |  |
| 1 | 6.3 (103/1534) |  |  |
| 2 | 7.6 (124/1514) |  |  |
| 3 | 8.8 (154/1598) |  |  |
| 4 | 9.7 (160/1493) |  |  |
| 5 | 7.4 (26/323) |  |  |
| **Geopolitical zone** |  |  |  |
| North-Central | 8.8 (120/1248) |  |  |
| North-East | 7.0 (97/1294) |  |  |
| North-West | 12.1 (217/1579) |  |  |
| South-East | 4.3 (52/1155) |  |  |
| South-South | 4.3 (37/815) |  |  |
| South-West | 7.8 (81/1087) |  |  |
| 95% CI= 95% confidence interval  \* Pearson’s chi squared test | | |  |

ADD IN GRAPH WITH SEXUAL AND ASEXUAL PREVALENCE

Figure 9: Significant positive correlation between asexual and sexual malaria parasite prevalence in each state. 95% CIs are shown.

Sexual parasite densities ranged from 2 to 10,570 parasites/μL, which is a much smaller range than the asexual densities. The geometric mean sexual parasite density was 81 parasites/μL (95%CI: 73-90 parasites/μL), which is significantly lower than the asexual parasite density (p<0.001). There was no significant difference between the geometric mean sexual parasite density between males/females (Table 4).

The geometric mean sexual parasite density was highest in the North-Central and lowest in the North-West (94 and 65 parasites/μL respectively)(Table 4). When looking at the association between sexual parasite density and geopolitical zone there was no evidence of a difference (p=0.36). Similarly, when stratified by age, the geometric mean sexual parasite density was very similar across all age groups (Table 4). The youngest age group did not have a significantly lower density of sexual parasites as compared to the older age groups, which is in contrast to the asexual density findings.

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| Table 4: Geometric mean sexual parasite density by sex, age and geopolitical zone in 2018 | | | |
|  | **Geometric mean sexual parasite density (parasites/μL)** | **95% CI (parasites/μL)** | **p-value** |
| **Sex** |  |  |  |
| Male | 85 | 74-98 |  |
| Female | 77 | 66-90 | 0.33\* |
| **Age (years)** |  |  |  |
| 0 | 71 | 47-107 |  |
| 1 | 89 | 69-114 |  |
| 2 | 91 | 70-118 |  |
| 3 | 65 | 54-79 |  |
| 4 | 90 | 74-110 |  |
| 5 | 80 | 45-141 | 0.23\*\* |
| **Geopolitical zone** |  |  |  |
| North-Central | 94 | 75-119 |  |
| North-East | 89 | 66-121 |  |
| North-West | 77 | 65-91 |  |
| South-East | 69 | 48-98 |  |
| South-South | 75 | 48-117 |  |
| South-West | 79 | 60-104 | 0.63\*\* |
| 95% CI= 95% confidence interval  \* Mann-Whitney test  \*\* Kruskal-Wallis test | | |  |