Climate change and the dynamics of age-related malaria incidence in Southern Africa: A focus on Zambia

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Abstract

In the last decade, many malaria-endemic countries, like Zambia, have achieved significant reductions in malaria incidence among children <5 years old but face ongoing challenges in achieving similar progress against malaria in older age groups. In parts of Zambia, changing climatic and environmental factors are among those suspected factors behind high malaria incidence. Changes and variations in these factors potentially interfere with intervention program effectiveness and alter the distribution and incidence patterns of malaria differentially between young children and the rest of the population. We used parametric and non-parametric statistics to model the effects of climatic and socio-demographic variables on age-specific malaria incidence vis-à-vis control interventions. Linear regressions, mixed models, and Mann-Kendall tests were implemented to explore trends, changes in trends, and regress malaria against environmental and intervention variables. Our study shows that while climate parameters affect the whole population, their impacts are felt most by people aged ≥ 5 years. Climate variables influenced malaria substantially more than mosquito nets and indoor residual spraying interventions. We establish that climate parameters is negatively impacting malaria control efforts by exacerbating the transmission conditions via more conducive temperature and rainfall environments, which in turn are exacerbated by cultural and socioeconomic exposure mechanisms. We argue that an intensified communications and education intervention strategy for behavioural change specifically targeted at ≥ 5 aged population where incidence rates are increasing, is urgently required and call for further malaria stratification among the ≥ 5 age groups in the routine collection, analysis and reporting of malaria mortality and incidence data.

Keywords: Climate change; Temperature; Malaria interventions; Age; Bayesian models; Zambia

Nomenclature for equations used

φ	Random effects
$\rho s,\ \rho \mathcal{T}$	Dependence parameters
$\mathcal{T}_i^2$	Temporary-varying variance parameter
W	Adjacency matrix
ψ	Latent component
$\mathcal{T}^2 Q(W, \rho s)^{-1}$	Variance
$\rho \mathcal{T}$	Temporal autoregressive parameter
α	Priori distribution
t	Time point

1 Introduction

Like many other Southern African countries, Zambia has made considerable progress in malaria mortality reduction in the last decade, achieving declines of up to 70% between 2010 and 2015 (Elimination8 Secretariat, 2019). However, in both mortality and incidence, this trend is not consistent across age groups (typically reported as <5s or ≥5). Trends in official published incidence rates show that there were subnational declines in most administrative districts (N = 72) during the period 2000–2008 before experiencing a sustained increase between 2010 and 2017 (of 43%) in both age categories (Kamuliwo et al., 2013; World Health Organization, 2018b). While over the whole of our study period (2000–2016), incidence rates in <5 children showed a 53% decline and those aged ≥5 had a 13% increase in malaria. Little has been done to consider age group targeted malaria intervention responses especially, among ≥5s, and most published studies and available data continues to be analysed for the <5 and ≥ 5 age group categories.

Among suggested reasons for increasing malaria incidence in several areas are mosquito resistance to dichloro diphenyl trichloroethane (DDT) used in indoor residual spraying (IRS); chemical pyrethroids in long-lasting insecticide nets (LLIN) (Chanda et al., 2011; Loewenberg, 2018; Manyando, 2016); population movement (Searle et al., 2017), and environmental factors driven by climate change (Bennett et al., 2016; Manyando, 2016).

Trends in temperature and rainfall, especially in regions of extreme climate diversity (Yue and Hashino, 2003), are often studied to detect significant spatiotemporal change (Adarsh and Reddy, 2015; Bisanzio et al., 2018; Drápela and Drápelová, 2011; Freeman and Bradley, 1996; Jaiswal et al., 2015; Jhajharia et al., 2013). However, few studies have examined comparative differences in how climate-induced ecological changes affect various population age groups vis-à-vis malaria communities. This is becoming ever more important given the recent trends in increasing rates for the ≥5 population. While the primary focus of intervention programmes, has been the highest risk <5 cohort, there remains a danger that, if left unattended, rates in the ≥5s could continue to rise resulting in considerable health and socio-economic burdens on communities. The economic consequences alone could be substantial, particularly if increases occur disproportionately in the younger economically active populations.

Studies have shown that the rates in some areas are being driven by the five to fifteen (Hast et al., 2019a, 2019b; Kapesa et al., 2018; Teh et al., 2018) and fifteen to twenty-five-year old cohorts (Bouyou-Akotet et al., 2014; Griffin et al., 2014; Nkumama, O'Meara and Osier, 2017; Pinchoff et al., 2016; Wotodjo et al., 2018) which supports concerns about the future long term economic impacts on communities through related impacts on economic productivity and capacity. However, with data generally being collected and reported in only two age categories it remains challenging to determine whether the reported increases in the ≥5 category rates are being driven by differentially higher rates in the five to fifteen category, the over forty fives or some other cohort in between.

It is predicted that in the near future, malaria will become an adult disease shifting from children to those older (Bouyou-Akotet et al., 2009; Brasseur et al., 2011; Brooker et al., 2017; Carneiro et al., 2010; Ceesay et al., 2008; Mawili-Mboumba et al., 2013). Possible reasons in support of this contention include successfully targeted intervention programmes at the very young along with various social, cultural, and economic behavioural factors, which increase exposure and reduce the uptake and effectiveness of interventions in the older age groups. What is still little understood and not been investigated to date has been the potential impact that changing climate and environmental variables may have on differential age-related incidence rates.

The study used malaria incidence data to explore the extent of influence that environmental variables have had on the observed increase in the incidence of malaria because of climate variables. This study follows on Bennett et al.'s (Bennett et al., 2016) relative effect of climate variability study on malaria incidence in 0-59-month-old children over four survey periods using sampled malaria survey data.

We investigated age-specific trends in malaria incidence in Zambia in relation to intervention programmes and climatic/environmental variables. Both <5s and ≥5 age-groups were investigated for i) the role of malaria control measures on the observed increase or decline of age-related malaria incidence without the impact of climate parameters; ii) the role of climatic parameters in the observed increase or decrease in malaria incidence without control measures; and iii) the role of climate in the observed increase or decrease in malaria incidence after adjusting for control measures.

2 Methods

2.1 Study area

Zambia is a country in South-Central Africa, with a typically tropical climate and approximately 18 million people living in an area of 752,000 sq. km (Central Statistical Office, 2013). The population is comprised of circa 20% of children <5 and 80% aged ≥5 years old. Based on a pre-analysis of rainfall and temperature variables, we classified seasonality to coincide with annual calendar quarters and to align with conventional transmission time lags. We then investigated "seasonality" based on mean seasonal shifts of up to one-month lag mainly via the seasonal onset of rains based on a recent study (Makondo and Thomas, 2020). Seasonality was synchronised according to annual quarters from January–March (Quarter One), April–June (Quarter Two), July–September (Quarter Three), and October–December (Quarter Four). The data is within the typical one to three months lag applied by many studies between the

variables and incidence reporting (Aal and Elshayeb, 2012; Darkoh et al., 2017; A. H. . Kilian, Langi, Talisuna and Kabagambe, 1999; Phung et al., 2016; Wu et al., 2016), suitable for our quarterly definition.

We applied computations of seasonal (quarterly) average trends detection and change-point analysis for maximum, minimum and mean temperatures (Tmax, Tmin, Tmean respectively), diurnal temperature range (DTR), mean rainfall, and maximum rainfall variables, to identify the presence of trends or significant climate variability points in the data. We obtained population data from national census reports and population estimates (Central Statistical Office, 2013). Data on malaria, and interventions were obtained from the National Malaria Elimination Centre, via the Ministry of Health (Chizema-Kawesha et al., 2010; Yukich et al., 2012).

2.2 Adjusting reported data for quality

Zambia health information records have more or less been comprehensive for the whole country since 2000 (World Health Organization, 2008), and the quality of data has improved even more since 2010 (President's Malaria Initiative, 2018). Nonetheless, we adjusted the data for varying quality using reporting rates, health-seeking, and data missingness. In the absence of specific information on district reporting completeness, this was estimated using information from malaria indicator surveys and/or demographic health surveys. All reports were aggregated quarterly.

Missing data values were imputed using multiple imputation methods via a trained Random Forest of observed values (missForest R package) (Stekhoven and Bühlmann, 2011), to replace missing values with plausible data values (Van Buuren, 2018). An estimate of 5% missing values was detected in our dataset. Treatment seeking information was extracted from demographic health surveys of 2001-2, 2007, and 2013-14 (Central Statistical Office, Central Board of Health, 2002; Central Statistical Office, Ministry of Health, 2014; Central Statistical Office, Centre, Zambia and Inc., 2009), then used to adjust for cases not seeking care or not captured by the health management information system.

The final calculation is denoted by Equation (1) (adapted from John Aponte) (WHO Malaria Policy Advisory Committee, 2018) summarising our final calculation of estimated malaria cases as:

$$= \left(\frac{Cases_{publicconfirmed} + \left(Cases_{publicpresumed} X TestPositivityRate_{public} \right)}{Reportingcompleteness} \right) / TreatmentSeekingRate \tag{1}$$

We did not have information on positivity rates; hence, we did not adjust for clinical malaria in the 2000–2008 dataset. This means that our conclusions may include some non-malaria fevers, which potentially could result in some malaria over-estimation.

2.3 Demographic, epidemiological and intervention data

Census and post-census populations and age-group (<5 and $\geq$ 5 years) estimates were obtained from the central statistics office (CSO) report (Central Statistical Office, 2013) and used to calculate district age-specific malaria morbidity and mortality rates. Routinely collected malaria epidemiological data were obtained from Zambia's Ministry of Health through the National Malaria Elimination Centre (NMEC). Malaria data for <5 and $\geq$ 5 years were reported collectively as clinical and microscopy or rapid diagnostic test (RDT) confirmed cases up until 2009. Since the countrywide introduction of RDTs (National Malaria Control Programme, 2012; World Health Organization, 2011; Yukich et al., 2012), clinical and confirmed cases have been reported separately (Mukonka et al., 2015).

We used continuous temporal (quarterly) environmental data, and district level routinely collected malaria data aggregated into a long-term series, disaggregated into <5s and $\geq$5 year old age-groups, across 17 years from 2000 to 2016. The use of two age groupings of malaria data have for the last decades been endorsed because children <5 years of age were and continue to be the most vulnerable group to malaria, accounting for over 60% of deaths worldwide (Murray et al., 2012; World Health Organization, 2018b, 2019). The specific focus on young children has also influenced the way malaria data is collected and officially reported. Typically, data is collated, analysed and presented either as <5s or $\geq$5s.

2.4 Intervention control data

Vector control data in the form of LLIN and IRS, which have been widely applied in recent years, were obtained from the national malaria elimination programme of Zambia (Chizema-Kawesha et al., 2010; Yukich et al., 2012). An operational coverage rate of two household residents per net was used (Masaninga et al., 2013; World Health Organization, 2008, 2015). The LLIN records were available from all distribution channels, such as antenatal and <5 clinics, the expanded program on immunisations, and from community-based and nation-wide mass distribution campaigns. We aggregated all data into 72 original districts to facilitate analysis of the full dataset over the whole 17-year study period.

2.5 Generating longitude and latitude representing population centres

Latitude and longitude coordinates were extracted to represent population-weighted centroids, with accuracy being validated in ArcGIS version 10. These locations were used to test for spatial autocorrelation and as spatial variables against malaria (see supplementary Fig. S1).

2.6 Climate and ecological data

Daily precipitation data (from Climate Hazards Group) with a spatial resolution of 5 × 5 km (Funk et al., 2015); temperature data (from NCEP Climate Forecast System Reanalysis) (Saha et al., 2012) with a 20 × 20 km of spatial resolution; and the 10 daily normalised difference vegetation index (NDVI) (from Copernicus Global Land Service) with 1 × 1 km spatiotemporal resolutions (Smets et al., 2018; Smets et al., 2013) were collected (see supplementary Table S1).

Our primary climate variable choices (temperature and rainfall) were based on literature evidence of how temperature and rainfall influence both short and long term changes in malaria transmission (Abiodun et al., 2016; Blanford et al., 2013; Colón-González et al., 2016; Krefis et al., 2011; Mohammadkhani et al., 2016; Odongo-Aginya et al., 2005; Okuneye and Gumel, 2017; Suk, 2016). Quarterly mean, maximum and minimum temperatures (Tmean, Tmax, Tmin, DTR) in ^{O}C, mean rainfall and max rainfall (mm) for the period from January 2000 to December 2016 were extracted using the R Program raster package (Hijmans, 2019) for all 72 districts. Diurnal temperature range (DTR) was computed from daily temperature data.

2.7 Modelling and statistics

To ensure model suitability and adequately detect patterns between malaria and environmental variables, we explored the data using simple regression, mixed methods, Ordinary Least Squares regression models (OLS), and the Bayesian Conditional Autoregressive (CAR) prior method. CAR models implemented spatiotemporal Generalised Linear Mixed Models (GLMM) for unique areas (Bennett, 2012; Mabaso et al., 2006; Reid et al., 2012) with inference in a Bayesian environment using Markov Chain Monte Carlo (MCMC) simulations. We applied Poisson data likelihood with an autoregressive hierarchy structure specified within its prior distribution to handle any spatial autocorrelation in the data using the CARBayesST R package (Lee et al., 2018).

The dependent variable used in the model is the Poisson data likelihood given that we chose a Poisson family over "Binomial" or "Gaussian" options. This model also suits the need to estimate the evolution of the spatial response surface of malaria over the considered time without coercing it to be the same for each period. This model has the capability of estimating the effect of risk factors such as temperature, rainfall, and NDVI on our response variables of malaria incidence or mortality (Lee et al., 2009; Wakefield, 2006). The model allows for spatio-temporal autocorrelation via random effects, which capture the remaining autocorrelation in the disease data after the effects of the known covariates have been accounted for. Therefore, we tested for the presence of spatial autocorrelation in our data set by first computing the residuals from a simple over-dispersed Poisson log-linear model that incorporates the covariate effects. These results showed that the assumption of independence is not valid for these data and that spatio-temporal autocorrelation should be allowed for when estimating the covariate effects.

2.8 Moran's I statistic for under-five malaria mortality

We used the Moran's I permutation test given the null hypothesis of no spatial autocorrelation and an alternative hypothesis of positive spatial autocorrelation. The Moran's I statistic gave −0·09 (p.value = 0·86), indicating the lack of evidence of unexplained negative autocorrelation in the residuals of our <5 age-group malaria mortality data. We, therefore, fail to reject the null hypothesis that there is no spatial autocorrelation in the values of death among <5 between January and March (first quarter) for this sample. Therefore, we assumed uncertainty in this data having spatio-temporal autocorrelation or independence and thence should allow for it during estimations in covariate effects. Preliminary results show varying levels of effect on <5 mortality risk by all covariates. However, none of these effects was significant at 95% CI.

2.9 The capture of spatio-temporal random effects

The model accommodates spatio-temporal autocorrelation into the response variable **Y** through latent random effects, through CAR-type prior distributions and spatio-temporal extensions. The symmetric nonnegative K × K neighbourhood controls the spatial units through the adjacency matrix $\mathbf{W} = (w_{kj})$, where W_{kj} characterises the closeness between a pair of spatial units (S_k, S_j). The weighted matrix creates higher values for area units with spatial adjacency, but low or 0 values for areas spatially apart. The matrix **W** creates a binary, ($w_{kj} = 1$ if spatial units (S_k, S_j) share a common boundary/edge and $w_{kj} = 0$ if not. However, this binary specification of **W** has to fulfil three conditions, namely; symmetry, non-negativity, and row sums greater than zero. This model treats spatially proximate areal units as spatially autocorrelated while those spatially apart (not sharing a boundary [$w_{kj} = 0$]) as conditionally independent (see (Lee et al., 2018) for more details). This model also captures the remaining autocorrelation in the data after accounting for the effects of known covariates. Spatial autocorrelation tests involved computing the residuals from simple over-dispersed Poisson log-linear models first. This model also incorporated covariate effects.

We then modelled the GLMM using spatiotemporal autocorrelation, via random effect structures from a conditional autoregressive prior distribution (Lee et al., 2018). We used this model to estimate the evolution of the spatial response surface of malaria from 2000 to 2016. The conditional multivariate model has a first-order spatially correlated precision matrix. We used this model to estimate the evolution of the spatial response surface of malaria from 2000 to 2015. The model specification is given by Equation (2):

$$\psi = \varphi_{kt,}$$

$$\varphi_t \big| \varphi_{t-1} \sim N\left(\rho T \varphi_{t-1,}\ \mathcal{T}^2 \boldsymbol{Q}(\boldsymbol{W}, \rho s)^{-1}\right) \quad t = 2, ..., N,$$

$$\varphi_1 \sim N\left(\boldsymbol{O},\ \mathcal{T}^2 \boldsymbol{Q}(\boldsymbol{W}, \rho s)^{-1}\right) \tag{2}$$

$$\mathcal{T}^2 \sim \text{Inverse} - \text{Gamma}(a, b),$$

$$\rho s,\ \rho \mathcal{T} \sim \text{Uniform}(0, 1).$$

The model $\varphi_t = (\varphi_{1t}, ..., \varphi_{Kt})$ represents a vector of random effects for period t, which progresses over time through an autoregressive multivariate process alongside the temporal autoregressive parameter ρT. The temporal autocorrelation, therefore, is induced through the mean $\rho T \varphi_{t-1}$, and the spatial autocorrelation by the variance $\boldsymbol{Q}(\boldsymbol{W}, \rho s)^{-1}$ respectively. Equation (3a) gives the statistical form of this matrix:

$$(\boldsymbol{W}, \rho s) = \rho s \left[\text{diag}(\boldsymbol{W} 1) - \boldsymbol{W}\right] + (1 - \rho s)\,\mathbf{I} \tag{3a}$$

In equation Two, 1 represents the K × 1 vector of 1's from the binary and the K × K identity matrix is denoted by I. While random effects are zero-mean centred, specific flat priors (ρs,ρT) and conjugate priors $(\mathcal{T}^2)$ are given and default values (a = 1, b = 0·01) for the latter (Lee et al., 2018).

We also compared these results with those from the generalised linear mixed models (GLMM) with a negative binomial (Brooks et al., 2017), (Nakagawa et al., 2017). Model results were compared using the Watanabe−Akaike information criterion (WAIC) (Watanabe, 2013), the deviance information criterion (DIC) and the log-likelihood (Gelman et al., 2014) for evaluating the predictive accuracy of our fitted models. The comparison helped us check for the best models, and enhanced robustness of the results because our malaria count dataset Y(t) and X(t) were collected at discrete times t∈{1, ...,n}, as denoted by the Equation (3b).

$$Y(t) = \mu + X(t) + \varepsilon(t) \tag{3b}$$

where μ is the mean value parameter, X(t) represents a stationary AR(1) process, with covariance cov(X(s),X(t)) = σ2exp(−θ|t−s|)cov(X(s),X(t)) = σ2exp(−θ|t−s|). The ε(t) is the measurement error term, with independently identically distribute (iid) as the normal i.e. N(0,σ_0^2).

The choice of our final models was based on their suitability following Zuur et al.'s protocol (Zuur et al., 2010) and partly using the DHARMa R package (Hartig, 2019) (see supplementary Table S2 and Fig. S2). We also computed the seasonal (quarterly) mean trend and applied change point analysis for all temperature and rainfall variables as the premise for determination of trend, change point, and subsequent impact.

We also used Cooks distance and residual diagnostic plots from linear models and other tests to determine which models were suitable for our dataset (Fig. S2). We implemented spatiotemporal mixed models, which accounted for spatiotemporal autocorrelation via random effects.

3 Results

3.1 Malaria spatial and temporal distribution and trends

Our analyses of current malaria trends since 2000 show an increasing overall trend in incidence among those aged ≥5 and a generally declining trend in <5s (Fig. 1). The trend for the <5s (Fig. 1(c)) has relatively and consistently been

declining (except for 2008 and 2009), while the average rising trend for the ≥5s (Fig. 1(d)) exhibits a very noticeable increase since 2008. Fig. 1(a) and (b) indicate that these incidence rates are not consistent across all districts and Fig. 2 (a–d) show that the trends are not consistent geographically across the country either. Supplementary Fig. S3 also shows that the proportion of malaria cases in <5s reduced from about 60% in 2000 down to ≈35% while that of the ≥5s increased from ≈40% to 65%.
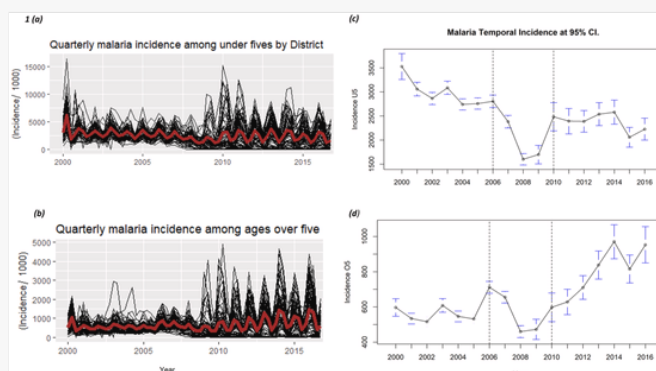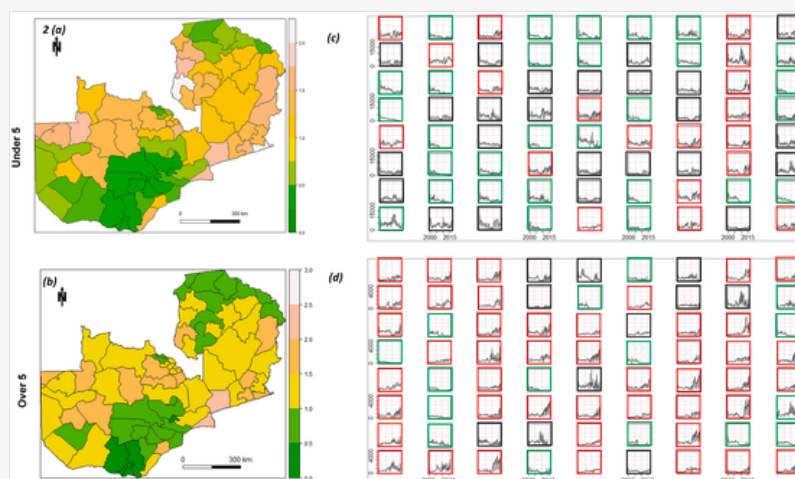

Individual district incidence and mean national malaria incidence trends in Zambia, 2000 to 2016. Fig. 1(a) and (b) show individual district incidence temporal trends while (c) and (d) show the mean temporal trend of incidence in Zambia from 2000 to 2016 among under 5 and over 5 years age groups.

District mean spatial patterns and individual district temporal trends 2000–2016. Fig. 2 (a) & (b) shows mean malaria incidence risk in maps among age groups under 5-years and over. Fig. 2(c) and (d) show Individual district Temporal distribution of malaria incidence among <5 children and >5 years. Each quadrant represents district incidence rates of one of Zambia's 72 districts from 2000 to 2016, while a Red outline indicates increasing incidence, Black = unstable, Green = declining. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

We then fitted generalised linear mixed models of Negative Binomial (NB) (2) using quadratic increases in variance with the mean (Brooks et al., 2017; Hardin et al., 2007). With district as the fixed effects parameter, the results accounted for dependence through random or fixed effect interaction parameters.

Table 1 summarises the results from our NB GLMM and the autoregressive (AR) GLMM models. The results show that the interventions (LLIN and IRS) have a stronger effect on incidence for the <5 than the ≥5s. LLINs had a weak negative correlation −0.08 (95%: -0·1, −0.06) among the <5s but a weaker positive correlation 0.03 (95%: 0·01, 0·06) in the older age group. IRS had a similar effect in the <5s, while the association was not significant in the older age group. Population density had the highest significant correlation coefficients across both age groups; −0.25 (95%: -0.38, −0.12) in <5s and −0.35 (95%: -0.43, −0.26) in ≥5s. In contrast, elevation, district latitude, and longitude (of population-weighted centroids – see supplementary Fig. S1) all had weak non-significant correlation coefficients. NDVI generally showed a strong significant positive correlation across both age groups (see Fig. 3 & Fig. S4 for detailed summaries of regression slopes).

Correlation coefficients and significance testing using negative binomial regression.

Variable	Incidence in under 5s	Incidence in over 5s	Incidence in all ages
LLIN	−0.08 (−0.1, −0.06)***	0.03 (0.01, 0.06)**	−0.02 (−0.04, 0)*
IRS	−0.08 (−0.11, −0.05)***	−0.01 (−0.03, 0.02)	−0.04 (−0.07, −0.02)**
Minimum Temperature	0.09 (0.06, 0.12)***	0.08 (0.05, 0.11)***	0.08 (0.05, 0.11)***
Maximum Temperature	−0.11 (−0.15, −0.07)***	−0.25 (−0.29, −0.21)***	−0.17 (−0.21, −0.14)***
DTR	−0.12 (−0.16, −0.08)***	−0.19 (−0.23, −0.16)***	−0.15 (−0.15, −0.19***
Population Density	−0.25 (−0.38, −0.12)***	−0.35 (−0.43, −0.26)***	−0.32 (−0.43, −0.22)***
Elevation	−0.08 (−0.22, 0.05)	−0.1 (−0.23, 0.04)	−0.1 (−0.23, 0.03)
NDVI	0.2 (0.17, 0.24)***	0.16 (0.13, 0.2)***	0.19 (0.16, 0.23)***
Mean Rainfall (mm)	−0.04 (−0.07, −0.01)*	−0.09 (−0.12, −0.06)***	−0.07 (−0.1, −0.04)***
Maximum Rainfall (mm)	−0.01 (−0.04, 0.01)	0.03 (0.01, 0.06)**	0.01 (−0.01, 0.03)
Latitude	0.03 (−0.04, 0.09)	0.01 (−0.05, 0.08)	0.03 (−0.03, 0.09)
Longitude	0.01 (−0.03, 0.06)	−0.03 (−0.08, 0.01)	−0.01 (−0.06, 0.03)

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1.

alt-text: Fig. 3

Fig. 3
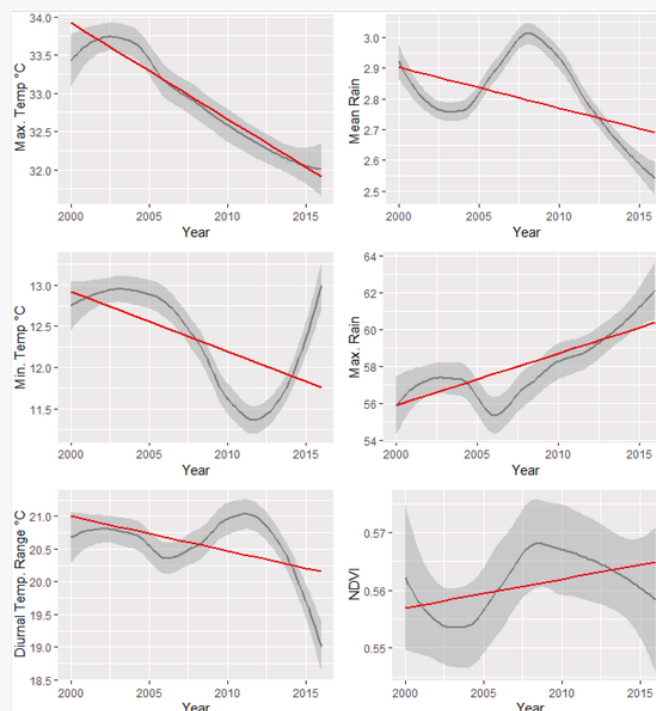
Summaries of overall temporal trends of environmental variable from 2000–2016 using LOWESS model. Grey represents confidence intervals (95% CI) with 75% data. The red-line represents a linear best fit of the distribution. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Having excluded mean temperature due to multicollinearity, we used only minimum and maximum temperature or DTR in our models. The maximum temperature showed a significant negative correlation −0.17 (95%: -0·21, −0·14) to malaria incidence across both age categories, whereas minimum temperature had a positive 0.08 (95%: 0·05, 0·11) correlation. Similarly, DTR had even stronger significant negative −0.15 (95%: -0·19, −0·15) coefficients in all ages (95%: -0·12 (95%: -0.16, −0.08) and −0·19 (95%: -0.23, −0.16) among <5s and ≥5s respectively). Finally, mean rainfall was negatively correlated −0.07 (95%: -0·1, −0·04) to malaria incidence across both age categories while

maximum rainfall was positively correlated, but was only significant 0.03 (95%: 0·01−0·06) in the older age group (see Table 1 and Fig. 4(a) and (b)).
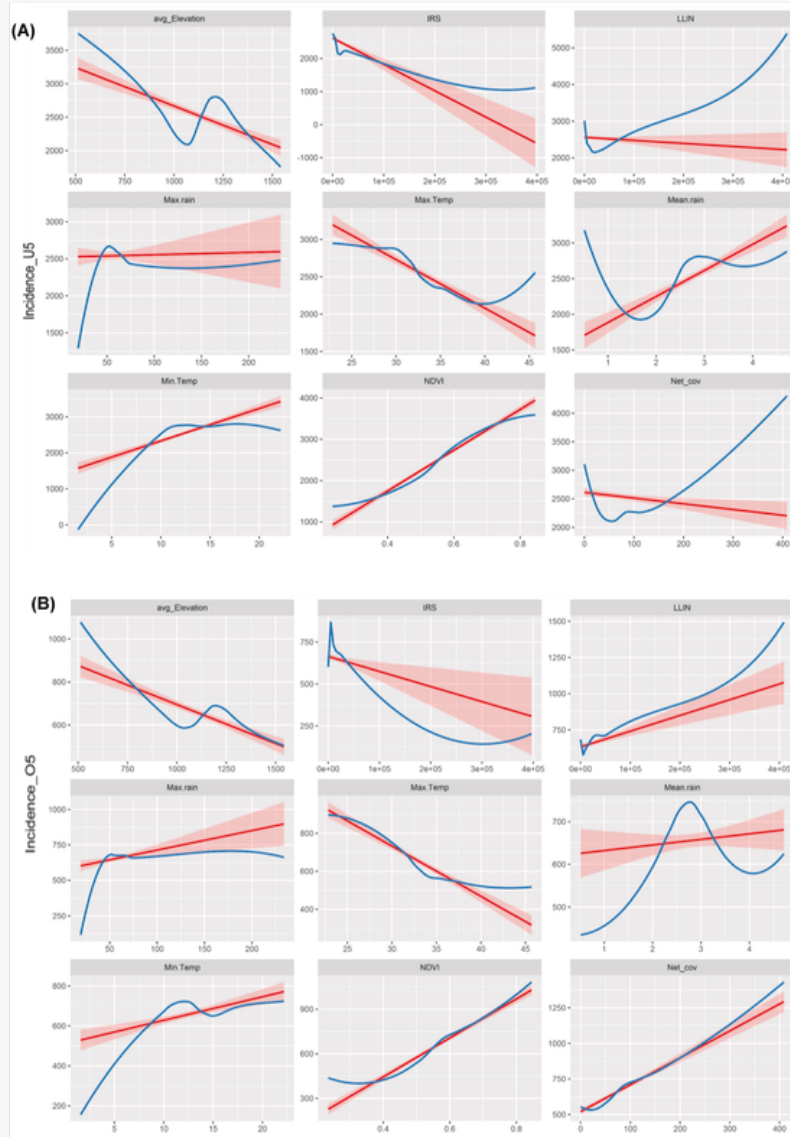
Regression slopes of the relationship between malaria, environmental and interventions by age. The Red-line represents a linear fit of the regression results, while the red-shade represents confidence intervals (95% CI). The blue-line represents the mean fit of the 75% data distribution. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

## 3.2 Impact of climate parameters and importance of interventions on current malaria distribution

Although, only mean rainfall showed a significant (95%) declining trend, temperature trends show declines in maximum −0.16 (−0.19,-0.13, adjusted $R^2 = 0·025$) and minimum temperature −0.11 (−0.14,-0.08, $R^2 = 0·011$). The observed trend changes in malaria along with those of temperature coincide with a switch and scale-up in nation-wide intervention programmes between 2008 and 2010, making it difficult to evaluate the specific effects of either environmental changes or interventions on changing rates in malaria.

In order to address this problem, we further modelled and visualised the effects of isolated climatic variables on malaria transmission, by fitting Bayesian models to compare predicted versus actual incidence rates while controlling for interventions and vice versa. For both age-groups, the results show that environmental variables had better model prediction accuracy (Fig. 5(a-f) and Fig. S5) and were better predictors exhibiting a stronger influence on malaria

transmission. We also report that environmental variables had better prediction accuracy in the ≥5 age group than in <5s, while models from interventions made better predictions in the <5 malaria rates (Fig. 5 (a-f) and Fig. S5).
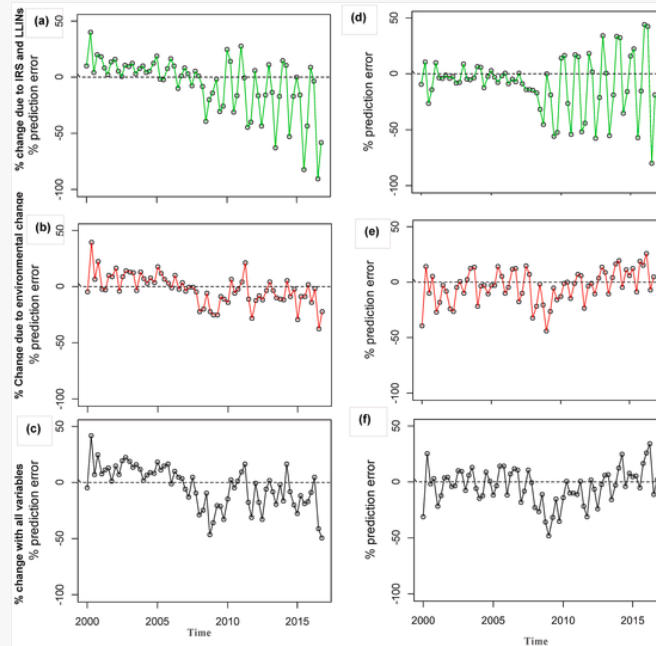
Percentage model prediction error by scenario. (a), (b) and (c) show model prediction error among children under-five years old. (c), (d) and (e) show model prediction error among people aged five years or older. Green line indicates results from models using intervention variables; Red line indicates results from models using environmental variables; Black line indicates results from models using all variables. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Although this effect was subtle between the period 2000 and 2006, from 2008 onwards, however, environmental variables are highly influential, with consistent prediction accuracy compared to interventions for the same period. The years 2007 and 2014 were characterised by a significant scale-up in nets (Fig. S6 using a 30% attrition rate (A. Kilian et al., 2011; Pulkki-Brännström et al., 2012; Tan et al., 2016) and may be associated with a significant decline in <5 malaria incidence in successive years.

In summary, modelling of predicted malaria cases using environmental variables and holding LLIN & IRS constant showed a much higher positive impact than when we held environment constant. However, as indicated earlier, environmental effects on post-2006 intervention predictions have lower variance and mostly high off-season incidence and low peak-season incidence (Fig. S7). Predicted values from all variables combined were similar to actual observed malaria while predicted values using only environmental variables were more accurate than those modelled from interventions alone. Environmental variables had more influence on incidence than interventions, and their respective models also had relatively lower prediction accuracy and better comparative model performance using DIC, WAIC and the loglikelihood (Fig. S4 and Tables S3). While the temporal trends of temperature were not statistically significant in themselves, they did suggest that changes in intra-periodic variability of temperature range might well be an essential factor. Tables S3 show results of six models (three for <5 and ≥ 5 age groups) using interventions variables, climatic variables and all variables combined.

4 Discussion

The results presented in Figs. 1 and 2 and S5, despite discordances in trends between mortality and incidence, form the backdrop for Zambia's current malaria policy agenda. However, the policy does not include any age-specific guidelines, apart from the World Health Organisation recommendations for LLINs and intermittent preventive therapy for infants (IPTi) and pregnancy (IPTp), coupled with effective treatment of malaria infections following prompt diagnosis (World Health Organization, 2018a). Furthermore, the inclusion of both adjusted clinical and confirmed malaria to derive malaria's true burden in the areas under study follows the available evidence in the literature.

Q2 For Zambia, several studies (Mukonka et al, 2014, 2015; Pinchoff et al., 2015, 2016) support the use of clinical data through their results which show high consistency in malaria incidence rates reported from both adjusted clinical data as well as study-based cross-sectional and longitudinal cohort surveys, and malaria indicator surveys. For instance, based on adjusted clinical and confirmed malaria, Mukonka et al. (2014) report ≈50% incidence rates in the Nchelenge district in 2012. RDT based diagnosis reported similar incidence rates of about ≈50% from cross-sectional and longitudinal

cohort studies (Pinchoff et al., 2015, 2016). This indicates how consistent the information provided by adjusted clinical malaria data is in calculating malaria's true burden without suffering from severe spatial biases and supports the use of clinical diagnosis data in this study.

The reported corresponding change in overall incidence rates with the significant rise in minimum temperature post-2010, and an observed decline in maximum temperature, confirm the significance of the relationship between temperature and malaria. We found that an increase in minimum temperature causes a subsequent rise in malaria, as does a decline in maximum temperature. This validates the observed trends in malaria; especially post 2010, where significant environmental changes tend to favour a more suitable transmission range (Figs. 3, 4a and b). The increasing minimum temperatures towards less extreme lows are favourable for higher malaria transmission, as is a narrowing DTR. These reported changes are further supported by the decline in the DTR in many districts and increasing malaria incidence trends in both age-groups, similar to those found elsewhere (Bennett et al., 2016).

DTR had a stronger independent association with the ≥5s age group (−0·19) than the <5s (−0·12), both being statistically significant (95%). The decline in maximum temperature and the corresponding increase in minimum temperature result in the observed decline in the DTR. The result is a move towards longer malaria transmission seasons and shorter malaria off-peak seasons. It may also result in an all-year-round transmission cycle in some areas. The observations here support the conclusion that ≥5s have a stronger significant association of increasing malaria incidence and risk with DTR and a higher environmental risk exposure than children <5 years old. Our findings support the call for further malaria stratification among the ≥5 age groups as shown in other study findings of malaria mortality (Dondorp et al., 2008) and incidence (Gerardin et al., 2015; Griffin et al., 2014).

Taking age into perspective might imply that few people among the ≥5s are actively using the LLINs. It was also clearly shown that IRS was more effective than LLINs among the ≥5s. Factors affecting this may include higher adult exposure to vector mosquitoes especially during extended working hours (i.e. economic influences), and spending evening times (peak biting hours) outdoors (i.e. social factors) compared to younger children. High LLIN misuse predominantly by fishing communities (Baume et al., 2009; Brieger, 2017; Eisele et al., 2011; Minakawa et al., 2008), high resistance of mosquitoes to pyrethroids (Chanda et al., 2011; Loewenberg, 2018; Manyando, 2016), low exposure to IRS due to targeted coverage and low LLIN usage thresholds despite high ownership (Brieger, 2017) especially among poor households have all been reported to undermine the expected protective effects of LLINs. Such information, where available, and in association with appropriate monitoring of environmental factors, may further help us understand the source of limited intervention effectiveness in different parts of the country.

The decrease in the <5 incidence may be an indication that a more comprehensive and effective implementation of interventions in this target population is required. The converse may also partly explain the increase in malaria among ≥5s whereby, culturally, at the household-level priority and effort is given to the implementation of intervention measures among the <5s and pregnant mothers relative to the ≥5s. Hence, an observed delay in disease onset from initially protected <5s leads to more disease episodes happening later in older ages when culturally and practically they become a lower priority. Such challenges undermine the expected positive effects of interventions from materialising in the older age group. Consequently, an intensified communications and education intervention strategy for behaviour change that targets a more active and aggressive uptake of interventions among the ≥5s is urgently required.

As malaria transmission intensity and incidence are still at least five times higher in the <5s than the ≥5s, careful consideration must be taken to monitor the transmission dynamics among the ≥5s, taking account of region-specific socio-economic and cultural nuances. If left unchecked, the rate of transmission increase observed in Zambia during the study period could soon pass that of the <5s. Should this happen, it would have significant direct economic and social impacts on local communities, where the economically productive population would directly carry the burden.

Other studies have reported small-scale movement patterns during peak biting hours, frequently among <18-year-olds (Hast et al., 2019a, 2019b), and higher RDT positivity odds (8·8) among 5-17-year-olds (Hast et al., 2019a, 2019b; Pinchoff et al., 2016), as inferred effects of delayed malaria onset. We can conclude that the ≥5s are often highly exposed to environmental risk through everyday activities to and from high-risk environments. This is especially true for those engaged in fishing, farming or the school age-group who spend most of the time in risky areas outdoors (Hast et al., 2019a, 2019b; Pinchoff et al., 2016) and are less likely to sleep under bed nets that are prioritised for children <5 years old.

According to the World Malaria Report (World Health Organization, 2018c), all East and Southern African countries, with the exception of Ethiopia, showed an increase in the incidence of malaria between 2010 and 2017. For the region as a whole, total malaria cases for all age groups increased by 10.7%; while they declined by 7.5% among the under-fives and increased by 23.1% in the over fives. This significant increase in infections among the older population accounted for circa two thirds of all recorded cases.

Other studies corroborate these findings, highlighting that currently, malaria incidence is increasing with age (Chilanga et al., 2020; Roberts and Matthews, 2016; Zgambo et al., 2017). Mwendera et al. (2019), highlights the challenges facing programmes as a consequence of the failure to understand the prevailing sociocultural environments affecting the

uptake of malaria control interventions. Other countries like Zimbabwe (Mutsigiri et al., 2017), South Africa (Gerritsen, Kruger, van der Loeff and Grobusch, 2008), Malawi (Chilanga et al., 2020), Mozambique and Uganda (Eisele et al., 2009; Mugisha and Arinaitwe, 2003) also report similar trends.

In Zimbabwe, for example, the incidence of malaria was initially higher in under 5 children before 2007, but higher from 2008 onwards in the over fives (Mutsigiri et al., 2017). More recently (between January and April 2020), Zimbabwe experienced unprecedented malaria outbreaks in over 200 locations causing over 250,000 infections and nearly 250 deaths (World Health Organisation (WHO), 2020). Over 90% of the infections during the outbreak were among those aged five years and over, indicating a strong shift in vulnerability between two the age groups.

The findings of our study, supported by the contemporary evidence elsewhere in the region, helps explain some of the regionally observed trends and patterns in Zambia over the last two decades and supports the growing body of evidence that there is a very real and potentially impactful increasing risk in older populations in malaria endemic countries.

Our findings strongly suggest the need for more granulated disaggregation of age groups in the routine collection, analysis and reporting of malaria data. The introduction of data reporting protocols in 5–17 and ≥ 18-year-olds would capture the 40% school-going population, and the more economically active population, respectively. School-based interventions show great potential in the reduction of anaemia, and the risk of Plasmodium infections, and as such are a potentially cheaper alternative for addressing the high malaria burden among schoolchildren (Ayi et al., 2010; Clarke et al., 2017; Maccario et al., 2017; Staedke et al., 2018).

We have shown that climate parameters has, to a considerable extent, offset the impact and the expected effectiveness of interventions. This trend is likely to continue with the consequence of increasing the minimum scale and cost of interventions needed to achieve an adequate observable reduction in malaria incidence rates. Climate variables, particularly temperature, are becoming increasingly more suitable for malaria transmission in many areas, and can broadly explain the observed high and increasing malaria transmission rates in parts of Zambia.

While our analyses show that intervention measures like IRS and LLINs have not fully offset negative environmental influences, we note that, if adequately applied, they still offer considerable potential for optimisation of their impact where resistance is contained (Chanda et al., 2013), and high ITN use is encouraged. Thus, climatic parameters have a significant effect on malaria incidence, and the older population age groups are more affected because intervention measures are better implemented and applied amongst the <5 age group.

We did not examine model performance on individual districts to highlight which districts had better intervention or climatic models. However, these results from the reported effects of diurnal temperature range could still be extrapolated through groups of districts with increasing malaria vs those with declining malaria trends.

We believe that our study has captured the fundamental and underlying transmission dynamics between the two age groups and explained malaria incidence in Zambia's decade of success in reducing mortality. This information can help intervention program strategies to focus on and take advantage of periods of less suitable temperatures and rains by driving malaria rates down to unrecoverable levels using such tools as mass drug administrations.

5 Conclusion

Our study established that although <5 children remain at a higher risk of malaria, those aged ≥5 years have a consistently increasing risk, more so than previously thought and which, if ignored, could soon be a significant problem for Zambia and other similar southern African countries. Our results corroborate those of earlier studies on the <5s (Bennett et al., 2016) but highlight that people aged ≥5 years are being affected by climate change-driven transmission. Our findings also augment the information and evidence base that helps us to better understand the drivers behind the current spatial and temporal trends in malaria incidence in Zambia.

The findings show that although the fitted models in the earlier period had better predictive accuracy than those in the later period (especially in the intervention models), in all three sets of models, environmental variables had a stronger influence and were better predictors of malaria infections than interventions.

It is evident that even short-term environmental change plays a crucial role in driving high malaria transmission and must be considered when planning and implementing intervention programmes, especially for elimination purposes in low transmission contexts. We have shown that the influence of climate parameters on malaria at the sub-national level is real and must be an essential part of appropriate preparedness and remedial action against the disease in tandem with direct remedial environmental interventions. Finally, it should be noted that although climate parameters constitute only some of the numerous influencing factors, it should not be treated as the sole or primary factor in malaria transmission (Chaves and Koenraadt, 2010; Molyneux, 2014). Similarly, uncertainty regarding the magnitude of climatic impacts on malaria should not be a reason for neglect either!

Study ethical review

The study was reviewed by ERES ethics review board (approval number 2017-Sept-011) and was authorised by the National Health Research Authority.

Author contributions

JL conceived the study, prepared the data, contributed to the study design, analysed, interpreted, and drafted the manuscript; AJM supervised the analysis, interpreted, and critically contributed to the writing; YB supervised the analysis and participated in manuscript drafting; UH conceived the study design, contributed to data preparation, and contributed to writing; DK contributed to data preparation and editing of the draft; MYS contributed to the analysis, and manuscript editing; BH contributed to data collection and writing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2021.111017.

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> ⓘ The corrections made in this section will be reviewed and approved by a journal production editor. The newly added/removed references and its citations will be reordered and rearranged by the production team.

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Highlights

- Malaria interventions are effective in <5 children but less effective in the ≥5s.
- Climate change affects younger adults and productive age-groups more than children.
- Intervention impact improves with attention to socio-cultural and behaviour dynamics.
- Monitoring age-related malaria and interventions require more careful attention.
- Integrated climate and age-sensitive intervention planning is urgently needed.

Appendix A Supplementary data

The following are the Supplementary data to this article:

Multimedia Component 1

Multimedia component 1

alt-text: Multimedia component 1

Queries and Answers

Q1

Query: Please confirm that the provided email "Lubinda-j@ulster.ac.uk" is the correct address for official communication, else provide an alternate e-mail address to replace the existing one, because private e-mail addresses should not be used in articles as the address for communication.

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Q2

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