BMJ open
accessible medical research

Estimating the relative contribution of parasitic infections and nutrition for anaemia among school-aged children in Kenya: a subnational geostatistical analysis

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ABSTRACT

Objectives: To quantify geographical variation in the relative contribution of parasitic infections, socioeconomic factors and malnutrition in the aetiology of anaemia among schoolchildren across Kenya, thereby providing a rational basis for the targeting of an integrated school health package.

Design: Nationally representative cross-sectional survey data were collected using standard protocols. For all included children, data were recorded on haemoglobin (Hb) concentration and common parasitic infections (*Plasmodium falciparum*, hookworm and schistosomes) and socioeconomic indicators. Ecological proxies of malnutrition and food security were generated using Demographic and Health Survey and UN Food and Agriculture Organization food security data, respectively. Spatially explicit, multilevel models were used to quantify impact upon child Hb concentration.

Setting: Randomly selected schools in ecologically diverse settings across Kenya.

Main outcome measures: Mean Hb concentration adjusted for infection, nutritional and socioeconomic risk factors; associated risk ratios and adjusted Population Attributable Fractions (PAFs) for anaemia, by region.

Results: Data were available for 16 941 children in 167 schools; mean Hb was 122.1 g/l and 35.3% of children were anaemic. In multivariate analysis, mean Hb was significantly lower in boys and younger children. Severe malnutrition and interactions between *P falciparum* and hookworm infections were significantly associated with lower Hb, with greater impacts seen for coinfected children. The contribution of risk factors to anaemia risk varied by province: in 14-year-old girls, PAFs ranged between 0% and 27.6% for *P falciparum,* 0% and 29% for hookworm and 0% and 18.4% for severe malnutrition.

Conclusions: The observed geographical heterogeneity in the burden of anaemia attributable to different aetiological factors has important implications for the rational targeting of antianaemia interventions that can be included in an integrated school health programme.

ARTICLE SUMMARY

Article focus
- Cross-sectional haematological and parasitological school survey data for the period 2008–2010 in Kenya.
- Spatially explicit, Bayesian multilevel models quantifying impact of infection, nutrition and social risk factors on child haemoglobin (Hb) concentration and adjusted Population Attributable Fractions for anaemia by province.
- Implications of spatial heterogeneity in underlying Hb status and risk factors for cost-effective geographical targeting of school-based antianaemia interventions, including deworming, malaria control and school feeding.

Key messages
For school-aged children living in Kenya:
- *Plasmodium falciparum,* hookworm and schistosomes are all significantly associated with lower mean Hb, with the largest impact seen for coinfection with hookworm and *P falciparum*, emphasising the importance of parasitic infections in the aetiology of anaemia in African school-age populations.
- Poor food intake is suggested to be an important contributor to anaemia in school-aged children.
- There is pronounced geographical heterogeneity in the burden of anaemia attributable to these identified risk factors, underscoring the importance of appropriately targeting interventions.

Strengths and limitations of this study
- A large and uniquely detailed dataset coupled with a novel Bayesian modelling framework that allowed for simultaneous quantification of the mean shift in Hb associated with each risk factor, and subnational risk of anaemia in school-aged children attributable to risk factors.
- Dependence upon cross-sectional design and ecological data limits inference of causality; incorporation of individual, nutritional-related factors and iron status indicators would improve quantification of their involvement.

BACKGROUND

Children of school-going age (5–14 years) make up one-quarter of the population of subSaharan Africa,[1] and the proportion of these children attending school has never been higher, in large part due to the recent global and national commitments to universal primary education school enrolment.[2] Yet many children enrolled in school suffer from poor health and malnutrition and, as a result, are less likely to attend and complete school or achieve their full educational potential.[3] For example, up to 40% of 5–14-year-olds are estimated to be anaemic,[4][5] which can affect cognition and learning.[6][7] Anaemia also affects the health of older girls as they reach puberty, potentially impacting upon future motherhood and the nutrition of the next generation of learners.[8][9] Fortunately, a number of simple and cost-effective interventions are available to avert the burden of anaemia, including malaria control,[10][11] deworming,[12] iron supplementation[13][14] and school-feeding[15]—interventions which are increasingly delivered as part of an integrated school health package.[16]

Identifying the optimal combination of school health interventions requires reliable information on both the geographical distribution of anaemia and the relative contribution of different aetiological factors. A previous study of anaemia among preschool children in West Africa employed a geostatistical framework to interpolate estimates of anaemia among children aged 1–4 years collected through demographic health surveys (DHS), while incorporating ecological predictions of malaria and helminth infection. While this work helped to define the geographical distribution and limits of anaemia in the region, it did not quantify spatial variation in the risk attributable to different aetiological factors.[17] Here, we take advantage of uniquely detailed haematological data collected during a comprehensive, national school health survey conducted across Kenya between 2008 and 2010.[18] An initial analysis showed that the relative contribution of *Plasmodium falciparum* to anaemia varied according to malaria transmission zones.[19] We extend this to investigate the relationships between haemoglobin (Hb) concentration and common parasitic infections (including *P falciparum*, hookworm and schistosomes), socioeconomic indicators and proxies of malnutrition and food security for schoolchildren across Kenya. We use an innovative Bayesian approach that quantifies the mean shift in Hb associated with each risk factor, which we use to estimate subnational variation in the risk of anaemia in school-aged children attributable to malnutrition, malaria and helminths to define targets for integrated packages of school health interventions.

METHODS

School survey data

This study uses cross-sectional school survey data collected between September 2008 and March 2010 using standard protocols, described elsewhere.[18][20] In brief, 480 government primary schools were selected to provide a national assessment of malaria and anaemia among schoolchildren. In a random subset of 167 schools, stool and urine samples were also collected to assess the prevalence and intensity of helminth infections. At each school, 10 children plus 1 reserve of each sex were randomly selected from each of classes 2–6 from the children present that day. This captures children aged 4–16, although 80% of the included children were aged between 8 and 13 years. Selected children were asked to provide a fingerprick blood sample, which was used to assess Hb using a portable photometer (Haemocue, Angelholm, Sweden) and *Plasmodium* infection in the peripheral blood based on microscopy-corrected malaria rapid diagnostic test (RDT)[18] results, whereby slides were subsequently read for all RDT positives. Children in all schools were asked to provide stool samples which were examined for the eggs of intestinal nematodes (*Ascaris lumbricoides*, *Trichuris trichiura* and hookworm species) and *Schistosoma mansoni* using the Kato-Katz method. In schools on the coast, where *Schistosoma haematobium* is widespread, children were asked to provide urine samples which were examined by urine filtration. A questionnaire was administered to all pupils to obtain data on insecticide-treated net ownership and use, history of anthelmintic medication, key socioeconomic variables, household construction and education of the child's parent/guardian. School locations were determined using a hand-held Global Positioning System and classified as urban using an updated 2010 urban extents mask derived from GRUMP.[21][22]

Nutritional proxy data

Anthropometric and food intake data were not available for all of our study population, and we instead relied on ecological measures. Proxy data for macronutritional status in school-aged children were derived from the Kenya 2008–2009 DHS.[23][24] Anthropometric measurements were extracted for children ≤5 years and for women of childbearing age (ages 15–49; see table 1). For children ≤5 years, the reported proportion consuming food rich in iron (flesh and organ meat) in the past 24 h was also extracted. These indicators, which provide a general measure of nutritional status in the wider community, were geo-located to the centre of each sampling cluster. Bayesian kriging,[25] a geostatistical interpolation method that accounts for the error introduced by estimating the semivariogram model (a function of the variability in outcome against the distance separating observation points), was used to interpolate a distribution of possible values for each indicator to survey school locations. This was done by incorporating the full posterior distribution of the Bayesian semivariogram model, estimated using the Bayesian statistical software WinBUGS V.14.1 (Medical Research Council Biostatistics Unit and Imperial College London). The mean

Table 1 Definition of included anthropometric indicators, and population-based cut-off values for severity of malnutrition, as defined by the WHO

Anthropometric measurement		Severity of malnutrition (prevalence range for <6 years) (%)		
		Low severity	Medium/high severity	Very high severity
Stunting	Height-for-age Z-score–2 SD	<20	20–40	>40
Wasting	weight-for-height Z-score >–2 SD	<5	5–15	>15
Underweight	weight-for-age *or* BMI-for-age Z-score > –2 SD	<10	10–30	>30

BMI, body mass index.

predicted prevalence values were then categorised according to WHO-defined cut-off values for severity of malnutrition by prevalence range (table 1). See the technical appendix for further details.

Two additional indicators were used to describe general food availability at each school location: predominant source of livelihood (based on the 2010 FAO Livelihood zones[26 27]); and food security conditions at the time of the survey (based on the FAO Food Insecurity Severity Scale[27 28]). Both indicators were obtained from the Famine Early Warning System Network (FEWS NET; http://www.fews.net). Information on the intended provision of formal, government-run school-feeding programmes was abstracted from the Homegrown School Meals Programme (HGSMP) and the Emergency HGSMP 2010 registers provided by the Kenya Ministry of Education (*personal communication*).

Analysis

A schematic summarising the major steps in our analysis strategy is provided in figure 1. Hb levels were adjusted for altitude and individuals were classified as anaemic using age-specific and sex-specific cut-offs.[29] Children were classified as having medium/high-intensity hookworm infection if the infection intensity exceeded 100 epg, and medium/high-intensity *S haematobium* infection if the infection intensity exceeded 500 epg (both representing the top 10th percentile). Reported information on the ownership of household assets and

household construction was used to generate wealth indices using principal component analysis,[30] and the resulting scores were divided into quintiles.

The initial candidate set of predictor variables for univariate analysis included age, sex, relative socioeconomic status, education level of the household head, protective behaviours (bednet usage and deworming) and infection status with hookworm, schistosome and *P falciparum*, in addition to school-level ecological covariates including urban/rural location, predicted prevalence of anthropometric indicators in younger children and women of reproductive age, livelihood zone and food security status and intended provision of school-feeding. In order to select candidate variables for spatial multivariable analysis, univariate analysis was undertaken using logistic regression (criteria: Wald test $p<0.1$) using Stata 11.1 software (StataCorp). SE were adjusted for dependence between individuals within schools using a clustered sandwich estimator.[31] Backward-stepwise elimination was then used to generate a minimum adequate multivariate model; excluded covariates ($p>0.05$) were retested in the minimal model to confirm lack of association. Basic age–sex interaction terms were also investigated, but there was insufficient evidence that these improved the overall fit of the model.

Retained covariates were included in a spatial multivariable Bayesian mixed-effects linear regression model using WinBUGs 14.1. This model included individual and school-level ecological fixed effects and a

Figure 1 Schematic of adopted analysis strategy. The dual aim of this analysis strategy was to (1) model the impact of risk factors on the children's haemoglobin (Hb) levels, and (2) estimate the adjusted Population Attributable Risk Fraction (PAF) associated with important, modifiable risk factors. This process was repeated at each realisation of the Bayesian hierarchical model to provide posterior mean estimates and credible intervals for all parameters of relevance.
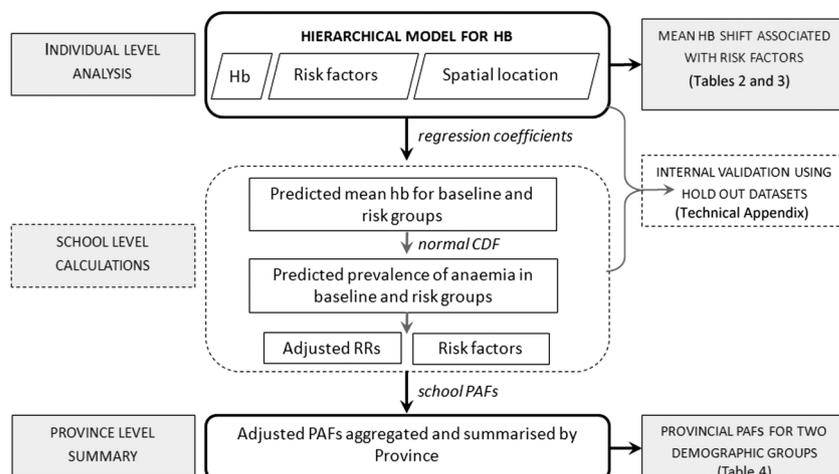
school-level geostatistical random effect (using an isotropic, stationary exponential decay function),[25] thereby incorporating a degree of spatial smoothing. Uncertainty in the predicted prevalence of anthropometric proxy indicators was incorporated by modelling these covariates as random variables with a β-distribution, defined using the prediction posterior distribution. At each model realisation, malnutrition was categorised as either low, medium/high or severe for each school location, according to table 1.

Given the large observed differences in mean Hb and prevalence of predictors by region and demographic group, adjusted Population Attributable Fractions (PAFs) for anaemia were estimated for two indicator demographic groups (boys aged 7 years, and girls aged 14 years) for each province in Kenya. In brief, at each model realisation, we estimated the prevalence of anaemia in each of the risk groups based upon the posterior mean and SD of the Hb distribution within each school. These were used to estimate (1) the relative risk of anaemia for each risk group compared with the baseline risk, and (2) the associated adjusted PAF, as described by Rockhill *et al.*[32] Estimates were subsequently summarised by province. Full statistical notations of Bayesian geostatistical modelling, PAF and model validation procedures are presented in the technical appendix. Model validation using hold out datasets, presented in detail in the accompanying technical appendix, suggests a very high degree of correlation at the school level between the observed and expected mean Hb levels ($R^2 > 0.98$) and the prevalence of anaemia ($R^2 > 0.95$), suggesting that the approach we used to estimate anaemia prevalence (and associated attributable fractions) was appropriate.

RESULTS

Data on Hb, malaria parasitaemia and helminth infection were available for 16 941 children (aged 5–16) in 167 schools (figure 2). The mean altitude-adjusted Hb concentration was 122.1 g/l, with 35.3% of children estimated to be anaemic. The spatial distribution of the unadjusted Hb data is presented in figure 2, summarised by school. There was significant geographical heterogeneity in mean Hb across the country (Moran's I p<0.001), with the lowest average levels observed in Coast Province
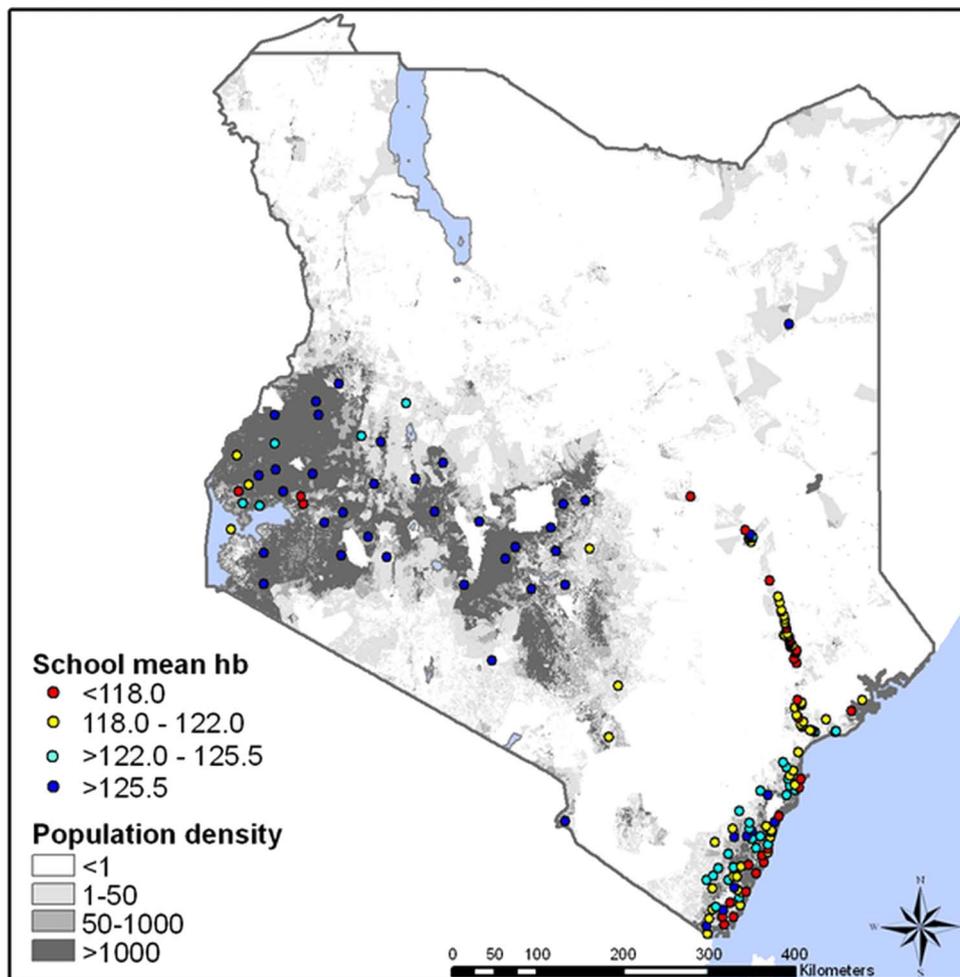

Figure 2 Spatial distribution of mean haemoglobin distribution across Kenya, by school. Hb is adjusted for altitude; population density (persons/km²) is shown for reference.

(120.1 g/l) and the highest in Central Province (134.0 g/l). Univariate analysis suggested that Hb levels increased with age and with relative socioeconomic status, and were significantly lower in individuals infected with *P falciparum* or medium/high-intensity helminth infections (table 2). Hb was also significantly lower in areas with predicted severe malnutrition, although there was no ecological relationship with

Table 2 Mean Hb concentration according to infection status, nutritional proxies and other characteristics in 16941 children aged 5–16 years (univariate analysis)

Variable	Data type and source	Children no. (%)	Mean Hb shift, g/l (SE)	p Value
Sex				
Female	Individual—KHS	8314 (49.1)	(vs female)	
Male	Individual—KHS	8627 (50.9)	−1.36 (0.28)	<0.001
Age (in years)	Individual—KHS	–	+0.89 (0.11)	<0.001
Socioeconomic indicators				
Educated household head *	Individual—KHS	8,333 (49.2)	+0.82 (0.41)	0.05
Household owns a mobile phone	Individual—KHS	10 065 (59.4)	+1.42 (0.40)	<0.001
SES quintile				
Lowest	Individual—KHS	3,272 (20.4)	(vs. lowest)	
Mid (quintiles 2–4)		9,926 (61.8)	+2.35 (0.50)	<0.001
Highest		2,854 (17.8)	+3.07 (0.82)	<0.001
Urban location	School-level—digital UE map	1,237 (7.3)	1.56 (1.52)	0.3
Current infections				
P. falciparum parasitaemic	Individual—KHS	607 (3.6)	−3.36 (0.77)	<0.001
Med/high-intensity hookworm (>100 epg)	Individual—KHS	931 (5.5)	−2.81 (0.69)	<0.001
Med/high-intensity *S. haematobium* (>500 epg)	Individual—KHS	799 (4.7)	−3.81 (1.02)	<0.001
Usually sleeps under a net	Individual—KHS	9,763 (57.6)	−1.78 (0.52)	0.001
Taken anthelmintic in the previous 6 months	Individual—KHS	7,494 (44.2)	+1.24 (0.48)	0.01
Nutritional proxies				
Wasting in under 5s (%)†				
Under 5%	Ecological—interpolated from	4,027 (23.8)	(vs <5%)	
5–15%	2008 DHS	10 257 (60.6)	−5.58 (1.04)	<0.001
Over 15%		2,657 (15.7)	−8.14 (1.21)	<0.001
Low BMI in adult women (%)†				
Under 20%	Ecological—interpolated from	12 867 (76.0)	(vs. <20%)	
Over 20%	2008 DHS	4,072 (24.0)	−1.98 (0.80)	0.01
Consumption of iron rich foods in under 5s (%)†				
Under 25%	Ecological—interpolated from	14 572 (86.0)	(vs. <25%)	
Over 25%	2008 DHS	2,369 (14.0)	+1.07 (1.24)	0.4
School-feeding (SF) status: ‡				
Not an SF district	School-level—MoE registers	3,690 (21.8)	(vs. not SF dist)	
SF district—no programme in school		8,417 (49.7)	−7.34 (1.08)	<0.001
SF district—programme in school		4,834 (28.5)	−4.80 (1.19)	<0.001
Generalised livelihood zone§				
Mixed farming	Ecological—FEWSNET	3,295 (19.5)	(vs. mixed)	
Pastoral and agro-pastoral		4,991 (29.5)	+1.11 (1.45)	0.4
Riverine and fishing		641 (3.8)	+2.08 (2.42)	0.4
Medium potential farming		4,073 (24.0)	−2.93 (1.13)	0.02
High potential farming		3,941 (23.3)	+1.37 (2.14)	0.2
Food security status¶				
Generally food secure	Ecological—FEWSNET	2,756 (16.3)	(vs. secure)	
Moderately food insecure		7,755 (45.8)	−3.20 (1.27)	0.01
Highly food insecure		6,048 (35.7)	−6.17 (1.25)	<0.001
Extremely food insecure		382 (2.3)	−5.12 (1.52)	0.001

*Household head educated to primary complete or above (reported).
†Interpolated from Kenya 2008/2009 DHS survey.
‡School included in either the Homegrown School Meals Programme (HGSMP) or Emergency HGSMP 2010 registers.
§Based on the USAID/FEWSNET Generalised Livelihood Zone 2010 Classification for Kenya.
¶Based on the USAID/FEWSNET Food Insecurity Severity Scale for the quarter corresponding to the KSH survey date.
DHS; Kenya Demographic Health Survey conducted in 2008/2009. MoE; Kenya Ministry of Education. FEWSNET; Famine early warning system network; KSH; Kenya School Health survey (conducted in 2008–2010).

predicted consumption of iron-rich foods. Univariate analysis also suggests a relationship between Hb and food availability, with significantly lower Hb levels in children living in very food-insecure areas.

Bayesian hierarchical model of Hb

Table 3 presents a multivariate analysis of factors associated with Hb levels. On average, boys had lower mean Hb compared with girls by 1.53 g/l (95% BCI 1.13 to 1.94 g/), and older children tended to have higher Hb levels, increasing by 1.08 g/l (95% BCI 0.99 to 1.17 g/l) with each yearly age interval. There was strong evidence for a multiplicative negative interaction between infection status and Hb levels, highlighting the health impacts of parasitic infections in school-aged children. Children with medium/high-intensity hookworm infection had Hb levels 1.03 g/l (95% BCI 0.02 to 2.00 g/l) lower than uninfected children, those with *P falciparum* 3.00 g/l (95% BCI 1.68 to 4.29 g/l) lower and *S haematobium* infection 1.75 g/l (95% BCI 0.60 to 2.92 g/l); children coinfected with both *P falciparum* and medium/high-intensity hookworm infection had Hb levels 5.56 g/l (95% BCI 2.67 to 8.64 g/l) lower than uninfected children.

Proxy measures of nutritional status were also strongly associated with Hb levels. Schoolchildren living in areas predicted to have severe prevalence of wasting had Hb levels that were on average 9.74 g/l (95% BCI 7.45 to 12.16 g/l) lower than those living in low-risk areas. School-feeding programmes also appear to have been targeted to districts with increased risk of anaemia, although examination of the 95% credible intervals suggests no statistical difference within target districts between the mean Hb levels in schools with and without intended provision of formal school-feeding programmes. Perhaps surprisingly, food security at the time of the survey (a qualitative measure that allows adjustment for acute conditions and the impact of seasonality) was not associated with Hb levels in multivariate analysis. Similarly, after accounting for all other factors in the model, relative socioeconomic status was not significantly associated with Hb levels.

The random effects variance components from this model indicate that most of the residual variation remains between children within schools: of the total unexplained variability in Hb, 13.8% occurred at the school level, while 86.2% occurred between children within schools. Closer examination of the spatial school-level random effect suggests that, after accounting for included predictors, most schools (81%) had similar Hb levels that could not be distinguished statistically (shown in green in figure 3). There was, however, some residual spatial clustering of schools with higher/lower than expected Hb levels (foci radii of ∼190 km, table 3) with significantly lower mean Hb levels observed in schools in the far south of Coast Province and in Nyanza and Western provinces (figure 3). Interestingly, a comparison of the observed prevalence of *P falciparum* and medium/high-intensity hookworm suggests that the prevalence of both infections was higher for these schools than for other schools in these provinces (*P falciparum* Kruskal-Wallis p=0.02; medium/high-intensity hookworm Kruskal-Wallis p 0.01). In contrast, the mean Hb levels were significantly higher for schools in the Rift Valley, Central and Eastern provinces.

Adjusted population-attributable risk fractions

Using the final Bayesian hierarchical model, we estimated for two demographic groups (girls aged 14 years,

Table 3 Bayesian hierarchical multivariate regression model for haemoglobin levels

Variable	Mean Hb shift (g/l)	95% BCI/SD
Baseline haemoglobin	117.3	(113.9, 120.5)
Sex (male)	−1.53	(−1.94, −1.13)
Age (in years)	+1.08	(+0.99, +1.17)
SES quintile (vs quintiles 2–4)		
Lowest	−0.56	(−1.14, +0.02)
Highest	0.25	(−0.31, +0.86)
Med/high-intensity *S. haematobium* (>500 epg)	−1.75	(−2.92, −0.60)
Med/high-intensity hookworm (>100 epg)	−1.03	(−2.00, −0.02)
P. falciparum parasitaemic	−3.00	(−4.29, −1.68)
Med/high hookworm—*P. falciparum* coinfection	−5.56	(−8.64, −2.67)
Wasting in under 5s (vs <5% prevalence)		
5–15%	−4.39	(−6.56, −2.09)
>15%	−9.74	(−12.16, −7.45)
School-feeding (SF) status:		
SF district—no programme in school	−2.14	(−4.76, +0.46)
SF district—programme in school	−2.78	(−5.43, −0.21)
Random effect terms		
Individual σ^2	183.6	(2.02)
Spatial σ^2 (school-level)	29.5	(7.93)
Range of spatial correlation (km)	194	(99318)

Figure 3 Graph of spatial random-effect (school-level residual) from the multivariate, Bayesian hierarchical model for Hb. Each point represents one school; the posterior mean is shown by the dot and the 95% BCI are represented by the error bars. The horizontal straight line in the middle of the graph represents the overall mean of the residuals, which are zero centred. Inset shows the school locations, shaded by the value of the school-level residual.
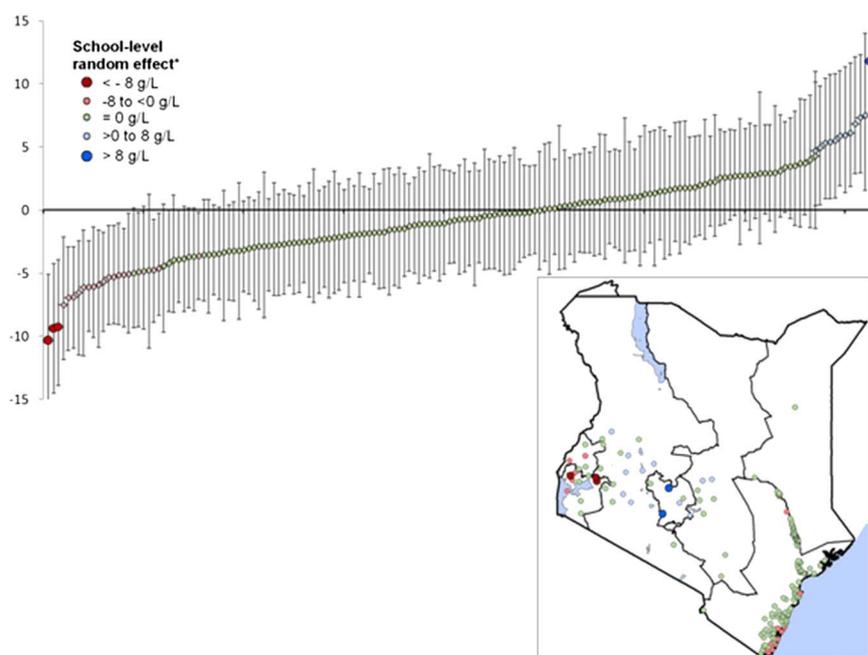
and boys aged 7 years) the PAF of anaemia due to *P falciparum*, medium/high-intensity hookworm infection, medium/high-intensity *S haematobium* infection, and acute malnutrition (prevalence of wasting in under 5s exceeding 15%) for each province in Kenya, adjusting for all other included predictors (table 4). Our results suggest that the relative contribution of each risk factor varies considerably by province. For example, in Coast Province, 13% (95% BCI 4% to 23%) of anaemia in 14-year-old girls attending school may be attributable to medium/high-intensity hookworm, comparing with 6% (95% BCI 2 to 10%) to *P falciparum* infection and 3.1% (95% BCI 0% to 8%) to schistosomiasis. Meanwhile, the results suggest that a reduction in acute malnutrition in Coast Province (to <5% wasting in ≤5s) would reduce anaemia prevalence by 19% (95% BCI 0% to 38%). This contrasts with Western Province, where the estimated risk of anaemia attributable to medium and high-intensity hookworm is 29% (95% BCI 1% to 55%) and to *P falciparum* 24% (95% BCI 0% to 41%); no schoolchildren in this district are exposed to *S haematobium* and acute malnutrition in under 5s is predicted not to exceed 5%. The wide 95% BCIs observed reflect (1) the smaller sample sizes for provinces other than Coast (given that N = schools, not individuals), and (2) the additional uncertainty surrounding proxies for

Table 4 Predicted adjusted population attributable risk fractions for key predictors across Kenya

	Population attributable risk fractions by province, % (95% BCI)					
	Central	**Coast**	**Eastern**	**Nyanza**	**Rift Valley**	**Western**
14-year-old girls						
Observed prevalence of anaemia	3.3	37.3	34.7	30.8	19.4	25.0
PAF for						
Med/high-intensity hookworm	n/a	13.0 (3.7, 23.1)	5.9 (0, 12.5)	8.2 (0, 30.0)	5.0 (0, 12.5)	29.0 (1.4, 55.1)
Malaria	n/a	5.8 (2.0, 10.4)	n/a	27.6 (0, 49.1)	n/a	23.6 (0, 40.9)
Schistosomiasis	n/a	3.1 (0, 0.08)	n/a	n/a	n/a	n/a
Acute malnutrition*	n/a	18.5 (0, 37.9)	18.4 (0, 73.0)	n/a	16.0 (0, 52.5)	n/a
7-year-old boys						
Observed prevalence of anaemia	5.0	43.3	23.2	43.2	22.4	19.2
PAF for						
Med/high-intensity hookworm	n/a	5.6 (1.0, 10.3)	n/a	11.0 (0, 21.6)	3.4 (0, 6.6)	13.5 (0, 27.5)
Malaria	n/a	1.5 (0.3, 6.1)	n/a	14.3 (0, 32.0)	n/a	15.8 (0, 28.1)
Schistosomiasis	n/a	0 (0, 5.5)	n/a	n/a	n/a	n/a
Acute malnutrition*	n/a	16.4 (0, 33.5)	16.4 (0, 67.1)	n/a	14.1 (0, 45.9)	n/a

Estimates are based on the predicted numbers anaemic in each risk group given by the mean and individual-level SD at each realisation of the Bayesian multivariate model for Hb, and are shown for two demographic groups by Province.
N/a, no children are exposed (ie, prevalence of predictor is zero in this demographic group).
*Exposure to 'acute malnutrition', prevalence of wasting in under 5s exceeds 5%.

malnutrition. Trends in PAFs observed for predictors in 7-year-old boys mirror those for older girls but are generally lower, a reflection of the lower baseline Hb levels in this group.

DISCUSSION

As global commitment and resources for school health and nutrition initiatives grow,[16] there is an urgent need to strengthen our understanding of the likely impact of interventions aimed at tackling important health and development outcomes such as anaemia. This requires a detailed understanding of the relative contribution of aetiological factors at policy-relevant scales. Here, we present a uniquely detailed national analysis of risk factors for anaemia among schoolchildren in 167 schools across Kenya. We introduce a new approach using multi-level linear modelling to provide a detailed description of the varying contribution of risk factors by administrative unit (province), while fully accounting for spatial variation in the underlying mean Hb. The results provide a vital decision-making tool for cost-effective targeting of the delivery of integrated packages of interventions tailored to each province, with the aim of reducing anaemia in schoolchildren. For example, school-feeding programmes in the Coast, Eastern and Rift Valley provinces may want to consider including iron-rich foodstuffs, while programmes in Nyanza and Western provinces, omitting malaria control initiatives, may not see the desired improvements in childhood anaemia.

Our analysis found evidence that *P falciparum*, hookworm and schistosomes were each significantly associated with lower mean Hb, observations consistent with current knowledge. Such findings corroborate recent results from the Global Burden of Disease study, which suggests that globally for anaemia 10.2% of years lived with a disability across all ages could be attributed to hookworm, 17.9% to malaria and 3.4% to schistosomiasis (Jasrasaria J, Murray CJL, Naghavi M. Global Burden of Disease 2010 Estimate: Strategy Report for Anaemia Envelope. (Unpublished report). Personal Communication 2012). Our analysis provides three additional insights into the epidemiology of anaemia. First, we confirm small-scale studies[33–37] that have suggested that coinfection with hookworm and *P falciparum* may have a multiplicative effect on the Hb level—effects which occur across Kenya. Second, we demonstrate pronounced geographical heterogeneity in the burden of anaemia attributable to identified risk factors. Associations for hookworm and *P falciparum* were most pronounced in Western Province, where the results suggest that together these two infections were attributable for close to 53% (95% BCI 1.4% to 96%) of anaemia cases in girls aged 14 years. Together, these findings emphasise the importance of parasitic infections in the aetiology of anaemia in school-aged children and underscore current efforts to control helminths and malaria as part of integrated school health programmes.[38 39] The PAFs provided here are useful for translating our findings into numbers that can

help policy decision makers appreciate the potential benefits of carefully targeted programmes tailored to each province that strike the best balance between dietary interventions, deworming and malaria control.[17 40]

Third, while acknowledging that we rely on proxy indicators, our results do suggest that poor food intake is an important contributor to anaemia in schoolchildren: the final model indicates that in communities where acute malnutrition is a severe public health problem (ie, where wasting in under 5s exceeds 15%), the mean Hb levels in school-aged children are on average 9.7 g/l lower than in well nourished communities, and as such eliminating acute malnutrition as a public health problem could avert close to 20% of anaemia cases in 14-year-old girls. This is consistent with the limited evidence from smaller individual-level studies suggesting an association between under-nutrition and anaemia in school-aged populations.[41 42]

Our spatially explicit hierarchical approach seeks to maximise the usefulness of these observational, cross-sectional data and the results show that while much of the between-school variation could be explained by included risk factors, a high degree of variation does still remain within schools. This suggests that there are individual-level factors beyond those measured that still need to be considered. In addition to individual iron status or food intake, there are a number of candidates. HIV infection is potentially likely to be a contributor, as even in asymptomatic HIV-infected individuals, anaemia is a common manifestation.[43 44] We were also unable to account for genetic traits such as sickle cell and other haemoglobinopathies,[45] or for the potential effect of menarche in adolescent girls.[46]

A number of additional study limitations should also be acknowledged. As we have previously acknowledged,[20] cross-sectional studies such as this are inevitably subject to a number of limitations including the potential of ecological fallacy, especially when incorporating population-level estimates. We acknowledge that our indicator of school-feeding (inclusion in the government school-feeding registers) is far from optimal and that the study would have benefited from detailed individual-level data on iron status and food intake. In addition, modelled associations are likely to be lower than the true impact, due to non-systematic measurement error in our infection indicators, which rely on single samples using standard parasitological diagnosis with <100% sensitivity.[47 48] Despite a robust stratified random sampling frame, our results may also be subject to some selection bias, as very ill children such as those with acute infections and severe chronic malnutrition may have been absent on the day of the school survey and thus not included in the study sample. Although contemporary regional or school-level attendance data are not available, the overall school attendance rates are known to vary geographically across Kenya.[49] For example, in 2005 (the most recent year for which subnational net primary school attendance figures are available), the reported

net attendance in Nyando District (Nyanza Province) was greater than 90% for both men and women, while in Turkana District (Rift Valley Province) the levels were between 30% and 40%.[49] If the Hb levels differ systematically between non-attending and attending school-aged children, this may act to either dilute or exaggerate geographical variation in Hb levels.

An additional factor that would influence individual-level variation is the onset of menarche in girls: no specific data were collected to record this, and the inclusion of a basic age-sex interaction term did not improve the model fit suggesting that more detailed information is required. Finally, this analysis is unable to account for the impact of recently cleared infections on current Hb status. The presented results represent a snapshot of the period 2008–2010 and it is conceivable that seasonality and intervention-related factors may have confounded the results. However, the inclusion of mosquito net use, recent deworming or food security (a seasonal covariate) in multivariate models did not improve model fits, suggesting that temporal and control factors were relatively unimportant.

CONCLUSIONS

A recent focus on schoolchild and adolescent health has emphasised the need to develop a deeper understanding of factors impacting health and development of this population group.[50–53] Here, we present a novel two-step process to model Hb levels and then predict the associated anaemia prevalence in different areas of Kenya. Our approach adds considerable value over and above what could be achieved by modelling anaemia directly, and the adopted geostatistical Bayesian framework allows for propagation of uncertainty associated at each step (including the generation of predicted ecological covariates) into the final confidence limits. Future expansion of this model could look at interpolating existing results to make predictions in non-surveyed areas, although this would require generation of values for all included individual-level covariates for each prediction location, increasing the prediction uncertainty. Our results highlight the marked geographical heterogeneity in the burden of anaemia attributable to identified risk factors in Kenya, which has major implications for effective targeting of packages of school-based interventions. We suggest that deworming can help tackle anaemia both in western and coastal Kenya, whereas malaria control is likely to have the greatest impact in western Kenya, while school-feeding programmes can help reduce anaemia in the Coast, Eastern and Rift Valley provinces. The priority now should be to explored in detail the health and educational impact of carefully designed integrated infection and nutritional interventions in this age group.

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