Role of malnutrition and parasite infections in the spatial variation in children's anaemia risk in Northern Angola

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Ricardo J Soares Magalhães[1*], Antonio Langa[2], João Mário Pedro[2,3], José Carlos Sousa-Figueiredo[4,5], Archie C.A. Clements[1], Susana Vaz Nery[1,2]

1 University of Queensland - School of Population Health, Australia. 2 Centro de Investigação em Saúde em Angola, Caxito, Angola. 3 Escola Superior de Tecnologia da Saúde de Lisboa, Portugal. 4 Liverpool School of Tropical Medicine, United Kingdom. 5 London School of Hygiene & Tropical Medicine, London, United Kingdom

INTRODUCTION

- Childhood anaemia is a severe public health problem in sub-Saharan Africa (SSA) affecting 67% or 83.5 million children in the region.
- Anaemia in children is associated with an increased risk of death, and may impair cognitive development, growth and immune function.
- Anaemia has a multifactorial aetiology and the major contributors include non-infectious (malnutrition, inherited haemoglobinopathies) and infectious causes.
- Infectious causes include: malaria, urogenital schistosomiasis, soil-transmitted helminthiasis (STH, caused by *Ascaris lumbricoides*, *Trichuris trichiura* and hookworms), among others.
- The prevalence of anaemia has been used as a measurable indicator for parasite control programme evaluation purposes because it reflects the aim of the control policy which is to control morbidity caused by these infections .
- The development of maps indicating the geographical risk profile of anaemia can help identify communities most in need and, if based on information on the major aetiologies of anaemia, allows an assessment of the risk of anaemia due to different causes .
- it is important to evaluate the consistency between an ecological approach and a complementary individual-level approach to modelling, by building spatial anaemia models using different modeling approaches.

- Using data from a recently, sub-national parasitological survey conducted in a meso-endemic area of Angola (Dande municipality in Bengo province), we built Bayesian geostatistical models of malaria (*Pf*PR$_{\leq 15}$), *S. haematobium*, *Ascaris lumbricoides* and *Trichuris trichiura* and predict small-scale spatial variation in these infections.
- The predictions and their associated uncertainty were used as inputs for a model of anemia prevalence to predict small-scale spatial variation of anaemia.

AIMS

1) quantify the role of factors associated with the geographical variation of anemia in children aged ≤15 years,
2) determine the geographical distribution of anaemia using an individual-level modeling approach and
3) provide the first high-resolution, local-scale anaemia risk map .

MATERIALS AND METHODS

Data source:

- Parasitological, Hb, questionnaire (age, sex, literacy, occupation, access to healthcare and history of previous treatment) and antropometric data were obtained from a baseline community-based cross-sectional survey conducted during May–August 2010 in three of five communes (Caxito, Mabubas and Úcua) in Dande municipality, Bengo Province, Angola, which are part of a Demographic Surveillance System (DSS) maintained by the CISA project (*Centre for Health Research in Angola*).
- Household information on type of flooring, ceiling and water, sanitation and hygiene (WASH) indicators was obtained from the CISA DSS data warehouse.
- A total of 972 households, distributed in 36 hamlets, were selected. Study participants included 960 mothers or caregivers (mean age 33.3 years, range 16–80 years) and 2,379 children (mean age 5.9 years, range 6 months–15 years).
- Electronic data for land surface temperature and rainfall for a 1 km × 1 km grid cell resolution were obtained from the WorldClim datawarehouse and the distance to lakes, rivers and irrigation canals was extracted for each sector in a geographical information system (GIS) . The geographical centre of the sector was linked to the environmental data to obtain values of the environmental variables using the spatial overlay procedure in the GIS.

Data analysis framework:

- Multivariable models of for each parasite infection built using the environmental variables as covariates and investigated residual spatial variation using semivariograms. This assessment revealed considerable residual spatial clustering, which justified modeling of second-order spatial variation using model-based geostatistics (MGB).

The subsequent analyses were conducted in two phases (**Fig. 1**):

- In Phase 1, we investigated the geographical variation of parasite infections in children aged ≤15 years using MBG.
- In Phase 2, we evaluated the impact of imprecise measurement of parasite infections on their effect sizes in relation to anaemia; estimated the PAF of anaemia due to malnutrition and parasite infections; and predicted the geographical variation of anaemia in children aged ≤15 years in the region using MGB.

Spatial models: **Fig. 1**

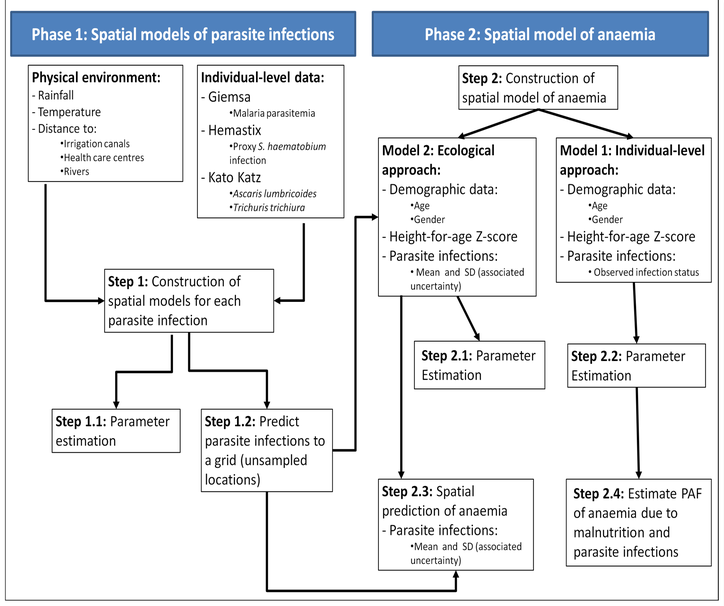
Model validation:

To determine the discriminatory performance of model predictions relative to observed prevalence thresholds the area under the curve (AUC) of the receiver operating characteristic was used. An AUC value of 0.7 was taken to indicate acceptable predictive performance.

Population attributable fraction of anaemia due to malnutrition and parasite infections:

Model 1 was used to estimate the risk of anaemia in children aged ≤15 years attributable to malnutrition and parasite infections . PAF estimates represent the fraction of total anaemia risk in the population that was caused by each aetiological factor, or alternatively, would not have occurred if the aetiological factor was eliminated, assuming the effects of other contributors (e.g., environmental variables) remain unchanged.

Fig. 1 Flow diagram showing the data sources and analytical steps of the analysis.



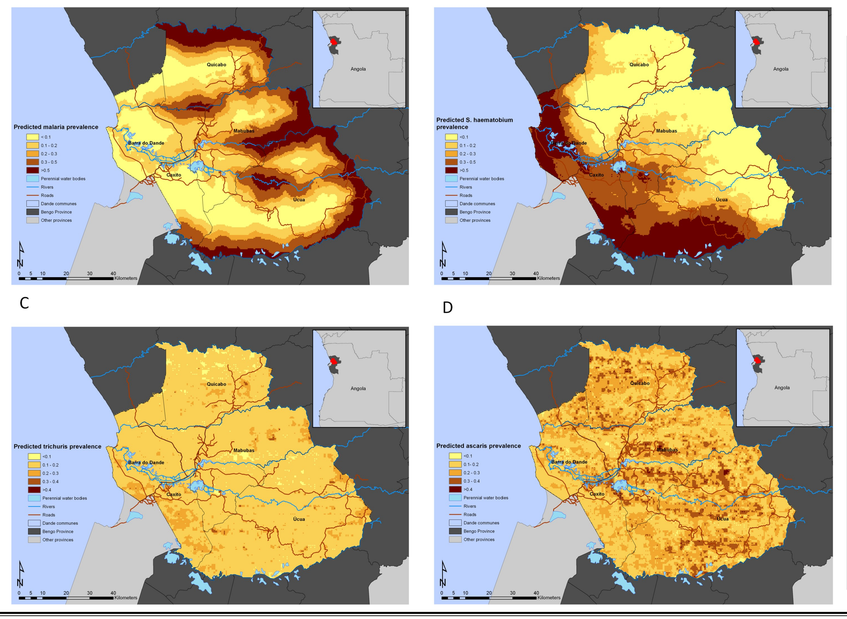
Results *1. Dataset for analysis*

Variable	Anaemia		Total
	No	Yes	
Hb concentration (g/L)			
Mean	12.2	9.7	11.2
Range (minimum-maximum)	11-15.9	3-10.9	3-15.9
Anemia prevalence			39.6 %
Age in years			1976
≤5	867	358	1,225
>5	314	437	751
Mean			
Gender			7 (3.7)
Male	558	423	981
Female	623	372	995
Height-for-age z-score <-2			
No	855	467	1,322
Yes	283	279	562
Stunting			30%
Weigth-for-age z-score<-2			
No	650	536	1,186
Yes	161	181	342
underweight			22.4%
Malaria			19.1%
No	1,009	588	1,597
Yes	172	207	379
***S. haematobium* infection**			13.0%
No	1,032	688	1,720
Yes	149	107	256
***A. lumbricoides* infection**			16.4%
No	966	686	1,652
Yes	215	109	324
***T. trichiura* infection**			10.8%
No	1,030	732	1,762
Yes	151	63	214

Table 1. Characteristics of children aged ≤15 years included in the analysis by anaemia (Hb<11.0 g/dL) status.

Results 2. *Geographical variation in parasite infections*

A **Fig. 2** Predicted spatial distribution of malaria (A), *S. haematobium* (B), T. *trichiura* (C) and *A. lumbricoides* (D) for the Dande municipality in Angola.



Environmental variables significantly associated with the parasite infections:

- Rainfall was positively associated with malaria and ascariasis and negatively associated with *S. haematobium* infection and trichuriasis, but only significant for *S. haematobium*.
- Land surface temperature was not significantly associated with any of the parasite infections .
- Distance to irrigation canals was significantly and negatively associated with *S. haematobium* infection only.
- Distance to health care centres was significantly and positively associated with malaria and
- Distance to rivers was significantly and negatively associated with malaria.
- Tendency for clustering (as assessed by the variance of spatial random effect) was highest for ascariasis and lowest for trichuriasis.
- The radii of the clusters of malaria, *S. haematobium* infection, ascariasis and trichuriasis were 24 km, 22 km, 26 km, and 27 km respectively

Results 3. *Spatial models of anaemia (table 2 & Fig. 3)*

Table 2. Spatial effects and population attributable fractions of chronic malnutrition and parasite infections on anaemia, in children aged ≤15 years in Dande province in Angola (CrI – Credible Interval)

Variable	Model 1 Posterior Mean (95% CrI)	Model 2 Posterior Mean (95% CrI)
Age	-0.22 (-0.26,-0.19)	-0.22 (-0.25,-0.18)
Female (vs male)	-0.17 (-0.38,0.04)	-0.17 (-0.38,0.03)
Height-for-age Z- score <-2	0.38 (0.15,0.61)	0.37 (0.13,0.60)
Prevalence of *Pf*PR$_{\leq 15}$	0.68 (0.38,0.99)	0.93 (-1.72,3.82)
Prevalence of *S. haematobium* infection	0.60 (0.26,0.94)	1.16 (-1.32,3.40)
Prevalence of *A. lumbricoides* infection	-0.16 (-0.45,0.13)	1.40 (-2.24,4.99)
Prevalence of *T. trichiura* infection	-0.27 (-0.61,0.06)	0.02 (-8.41,7.98)
Intercept	0.95 (0.40,1.61)	0.30 (-1.19,3.21)
Rate of decay of spatial autocorrelation (φ)	14.7 (5.36,19.84)	14.49 (5.36,19.78)
Variance of spatial random effect	0.41 (0.06,1.26)	0.76 (0.20,1.98)

- Age in years was significantly and negatively associated with anaemia risk
- Sex was not significantly associated with anaemia risk or stunting
- Model 1: *Pf* PR$_{\leq 15}$, and *S. haematobium* infections were significantly and positively associated with anaemia risk
- Model 2 none of these parasite infections was significantly associated with anaemia.
- Neither the prevalence of *A. lumbricoides* nor *T. trichiura* infection was significantly associated with risk of anaemia.

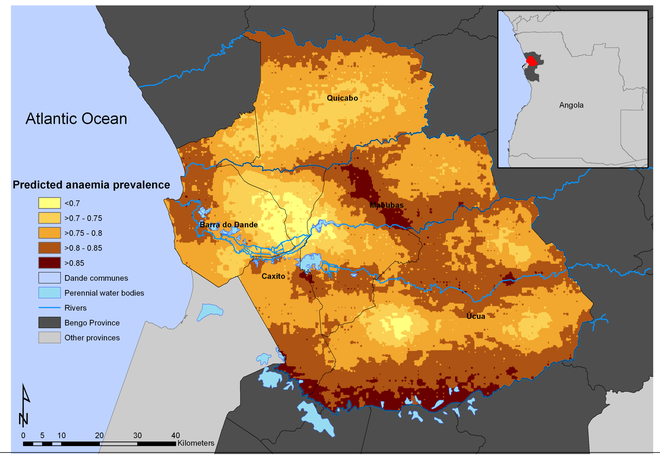


Fig 3. Predicted spatial distribution of anaemia (Hb<11.0 g/dL) in younger boys for the Dande municipality in Angola

Using Model 2, with an AUC of 0.82 (95% CI: 0.73-0.89).:

- The risk of anaemia was consistently high across the entire study area, with maximal prevalence (>85%) in small foci in Caxito, central Mabubas and in an elongated cluster in south Úcua in association with inland water bodies
- Larger foci of prevalence of anaemia between 80-85% were also predicted for northern Quicabo and areas adjacent to the inland water bodies in eastern Barra do Dande.
- Phi (φ) indicates the radius of the foci was approximately 22 km.

Results 4. *Risk of anaemia attributable to malnutrition and parasite infections*

Using Model 1, the estimated risk of anaemia in children aged ≤15 years attributable to

- stunting was 12.4%,
- *P. falciparum* was 15.6%, and
- *S. haematobium* was 9.7%.

DISCUSSION

- The predictive map of anaemia (Fig. 3), based on an ecological approach (mapped outputs from spatial models of malaria, *S. haematobium* and STHs), identifies the clusters of high anaemia risk and indicates that anaemia control should be prioritized to inland rural communities within the high endemicity areas (prevalence >85%).
- These areas correlated with larger areas where malaria risk is at its highest (prevalence >50%). Furthermore, high risk areas of *S. haematobium* (>50%) overlapped with high risk areas of malaria (>50%),
- These areas present opportunities for integrating malaria interventions with praziquantel delivery to reduce anaemia prevalence.
- In areas with high prevalence of helminth infection, and as part of deworming programmes, the distribution of micronutrients for the treatment of severe anaemia cases should be included and providing WASH with the aim of reducing the burden of anaemia attributable to helminth infections .

- Malaria, malnutrition and *S. haematobium* play a central role in anaemia burden in this region of Angola : almost 16% of anaemia cases in children aged ≤15 years could have been averted in 2010 by eliminating malaria in the population, 12% by eliminating malnutrition and 9.7% by eliminating schistosomiasis.

- The predictive anaemia map with measurement error suggests that in the absence of individually collected data an ecological approach may be a valid approach to identifying communities at highest risk of anaemia. Taking explicit consideration of the uncertainty of mapped values of parasite infection surfaces has contributed to a more detailed handling of prediction uncertainty.

- The comparison of an individual-level approach to anaemia modelling (whereby children's infection status was used as a measure of exposure) with a model in which infection status was assigned with measurement error (by spatial overlaying predicted parasite surfaces) suggests that measurement error in an exposure variable is likely to bias the estimates of regression coefficients towards the null as none of the effects of parasite infections in the model with measurement error were statistically significant.

Limitations:

- We have attempted statistical control of confounding by adjusting our analysis for age and sex. However, even if one uses adjusted estimates of the relative risk, PAF estimates can be biased in the presence of unaccounted confounding factors and overestimation of PAF can occur.
- Haemoglobinopathies and thalassemias, which are important inherited haematological conditions, were not incorporated in the models.

Ethics statement: *The study protocol was approved by the Angolan Ministry of Health Ethics Committee. All households that agreed to participate were enrolled in the study after handing in the signed consent form. Participants found to be infected with P. falciparum S. haematobium or S. mansoni were treated according to national guidelines.*

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