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Degree: MSc in Biostatistics

Title: Bayesian spatio-temporal analysis of malaria prevalence in children aged 2-10 years from 2000-2015 in Gabon

Abstract

Background: In Gabon malaria still threatens the health of children and the country's economic. In order to contribute in the estimation of malaria burden, in the endemic risk classification, and help in the design of the effective intervention, it is necessary to identify hot spots and cold spots, and to provide policy makers with good estimates of malaria prevalence at the national level with appropriate methods. It is also important, to understand, at a small spatial scale, how some factors are affecting the variation of malaria prevalence. This includes mainly geo-climatic factors, since malaria is related the meteorological conditions. This study focused on the effect of space and time in the distribution of malaria prevalence, and the effect of ecological variables in its variation for children between 2-10 years of age living in Gabon.

Method: This study used successive cross-sectional data carried out in four time points: 2000, 2005, 2010, and 2015, using a stratified two-stage sampling method. The survey data provided information on malaria prevalence for children aged 2-10 years, and cluster-level ecological variables. Descriptive analysis such as the mean of the prevalence and the covariates with their standard deviation, on average, overtime, by province and type of residence was carried out, followed by more advanced models for the estimation of the prevalence. Considering the weighting scheme, the prevalence was obtained via the space and time Horvitz and Thompson estimator. This was then smoothed using the Besage York Mollié (BYM) model with space-time interaction, to reduce uncertainty due to the small area. The spatial autocorrelation was determined using the Moran's I index, and hot spots with the local statistic Getis-Ord General Gi. The relationship between malaria prevalence and predictors was analyzed nationally. Ordinary Least squared (OLS) was used to see if the covariates can explain the spatial autocorrelation observed in the prevalence, Geographically Weighted Regression (GWR) or

Spatial Varying Coefficient (SVC) to evaluate if the relationship between prevalence-covariates was not varying by location. Spatio-temporal model for OLS (SPTOLS) was used to account for the effect of time and space, and Geo-Additive Model (GAM) for considering the non-linear relationships. Lastly, Spatial Lag Model (SLM), Spatial Durbin Error Model (SDEM) or Spatial Error Model (SEM), were used for identifying the spillover effects. These were implemented in the Integrated Nested Laplace Approximation (INLA) using Stochastic Partial Differential Equation approach (SPDE). The different methods were compared to find the best one fitting well the data by using the DIC.

Results: In total, 336 clusters were used, with 153 (46%), and 183 (54%) in rural and urban areas, respectively. On average, Estuaire province has the highest prevalence, followed by Moyen-Ogooue and Woleu-Ntem, 29% ($\pm 16\%$), 22% ($\pm 13\%$), 21% ($\pm 10\%$), respectively before the estimation using the smooth space-time model with sampling design. On average, after using the space-time smoothing model and the sample design, it was found that the prevalence decreased with year, and then showed a rebound from 2010. The highest value of the prevalence overtime was 46% in the Estuaire province in the year 2000 and the lowest value overtime was 6% in Ogooue-Maritime province in the year 2010. However, the effect of year was not significant. When the weight scheme was introduced, the variance of the estimate was reduced, and the contribution of the space in the variation of malaria prevalence was 46% during 2015. A strong spatial autocorrelation of the prevalence was found. Hot spots changed in magnitude by space and time, often in the north-west and the western part of the country. Cold spots were found mostly in the southern part. The spatial effect became almost null after 290 km (95% Credible Interval (CI): 230;360). The model including only the ecological variables was better in reducing the spatial variation. Using the SDEM, it was clearly seen how the prevalence can be influenced by the change of some risk factors in the nearby clusters or in the same cluster. The increase of malaria prevalence in a cluster was slightly and significantly associated with one-unit increase of: wet days (3%, 95% CI: [1%, 5%]) in the same cluster, and mean temperature (2%, 95% CI: [1%, 3%]) in the nearby clusters. It decreased slightly and significantly with a one-unit increase of day land surface (-2%, 95% CI: [-2%, -1%]) in the same cluster, but only slightly in the nearby clusters (< 1%). For a particular cluster, malaria prevalence decreased (-21%, 95% CI: [-40%, -5%]) greatly with the Insecticide Treated Bed

Nets (ITNs) coverage increases in the nearby clusters. In contrast to GAM using SDEM for ITNs coverage only, the relationship between malaria prevalence and ITNs coverage was clearly non-linear decreasing after 20% of coverage. Overall, malaria prevalence had non-linear relationship with mean temperature, night land surface temperature, enhanced vegetation index and rainfall.

Conclusion: Substantial progress has been made to slow down the spread of malaria in Gabon. However, malaria prevalence is still high, with important spatial variation and hotspots in its distribution. The distribution of hot spots was showing some changes overtime in the cluster of households. Including the spatial effect allowed to obtain more accurate estimate of the prevalence, hence a better estimation of the clinical burden of *P.falciparum*. This can allow a better allocation of resources.

From our findings, results may apply in two aspects: Firstly, in research focused on estimation in malaria. Such research trying to obtain an estimation of malaria outcomes, such as incidence, in different areas are encouraged to check on the spatial or spatio-temporal component in their estimation based on small area estimation with Bayesian approach due to the small level of unit to obtain more accurate estimate. Secondly, in strategies to reduce the prevalence. It is necessary to find strategies to increase, at the cluster of households level, the ITNs coverage to at least 20%, by taking into account some ecological variables implied in the decrease of the prevalence and to improve access to all health care interventions in the rural areas throughout the country.

Monitoring the vector control intervention and those ecological variables can contribute to strengthen the action of interventions in public health, because of the spillover effect, which can spread the benefit of intervention over long distance to reach several areas not targeted in the neighborhood. This effect contributes in the cost-effectiveness of the interventions. The national direction of meteorology (DGM) and the NMCP need to work together to mitigate or control adverse climatic change effect on malaria if possible by developing early warning system for malaria. These results can be considered as a baseline for future surveys investigating the malaria distribution in Gabon and elsewhere.