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Geoadditive Cox Models with Gaussian and Binomial Links for the Analysis of Wastingstatus of Nigerian Children

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Abstract
Malnutrition is associated with more than half of all children deaths worldwide. A study into geographical variability of nutritional status of children in Nigeria was observed from krigingand thecontinuous covariates weight for height (wasting) that exhibit pronounced non-linear relationships with the response variable was analysed. The Multiple Indicator Cluster Survey 3 (MICS3) data set contains several variables. Only those that are believed to be related to nutritional status were selected. All categorical covariates are effect coded. The child's age is assumed to be nonlinear; the state is spatial effect while other variables are parametric in nature. Wasting is higher among children in the urban areas, the more rich the parents the more prevalence of wasting. Mother's education is inversely associated with child's wasting. Sex of the child is not significant with wasting and severe wasting is prevalent in the Northern region of the country. The study builds a statistical model that will help various health agencies in the country in developing a framework, policies and programmes that will improve child health care.
Keywords: Wasting, Categorical data, Binomial,Gaussian, and Kriging

1.0 Background of the Study

Protein energy malnutrition is the second most important cause of childhood morbidity and mortality in Nigeria after infectious diseases. It is a direct cause of death in 2% of the children under the age of five years and an underlying factor in 60% of the more than 10 million child deaths that occur each year (WHO, 2002) The World Health Organization estimates that approximately 150 million children under five years in developing counties are underweight and an additional 200 million children are stunted (WHO 2000). The Millennium Development Goal is to reduce by half the proportion of peoplewho suffer from hunger between 1990 and 2015. The World Fit for Children goal is to reduce the prevalence of malnutrition among children under five years of age by at least one-third (between 2000 and 2010), with special attention to children under 2 years of age. A reduction in the prevalence of malnutrition will assist in the goal to reduce child mortality.(SOWC, 2007).In a well-nourished population, there is a reference distribution of height and weight for children under age five. The extent of under-nourishment in a population can be gauged by comparing children to a reference population. The reference population used in this report is the WHO/CDC/NCHS reference, which was recommended for use by UNICEF and the World Health Organization at the time the survey was implemented.

Previous studies on child mortality have focused on various socio-economic, demographic or health factors available in specific data sets but have mostly neglected spatial aspects Bayesian geoadditive survival models which deal with small area spatial effects, nonlinear and time-varying effects of covariates and usually linear effects by introducing appropriate smoothness prior for spatial and nonlinear effects. Since the survival time of children is measured in months which rely on discrete-time survival models, Bayesian Inference uses recent Markov Chain Monte Carlo (MCMC) simulation techniques, described in Farmeir and Lang (2001) and implemented in the open domain software BayesX, available from http://www.statuni-muenchen.de/-lang/bayesX. In a related work, Crook*et al* (2003) applied a geoadditive probit model for analyzing time to event data in a medical context.

The Cox proportional hazards model is a commonly used method when analyzing the impact of covariates on continuous survival times. In its classical form, the Cox model was introduced in the setting of right-censored observations. However, in practice other sampling schemes are frequently encountered and therefore extensions allowing for interval and left censoring or left truncation are clearly desired. Furthermore, many applications require a more flexible modeling of covariate information than the usual linear predictor. Further extensions should allow for time-varying effects of covariates or covariates that are themselves time-varying. Such models relax the assumption of proportional hazards. One of the main objectives of statistical modeling is to quantify the influence of variables (called covariates) on a measure of interest (the so called dependent variable or the response). A general framework to perform such analyses is provided by regression models which have been developed for a variety of response types. The most prominent regression model is the classical linear model, where the response variable y is assumed to be Gaussian-distributed and the covariates $x_{1,...,} x_p$which act linearly on the response.

1.1 Children Nutritional Status Models in History

When analyzing continuous survival times, the Cox proportional hazards model ($\lambda(t,v) = \lambda_0(t)\exp(v.\gamma)$) is the classical choice, if no parametric form for the distribution of the survival times can be assumed. While allowing for a flexible baseline hazard rate, the Cox model ($\lambda(t,v) = \lambda_0(t)\exp(v.\gamma)$) expects a parametric form for all covariate effects, which may be too restrictive in realistically complex applications. Several proposals for the analysis of such geoadditive survival data have been made in the past Henderson*et al,* (2002) proposed a Cox model with gamma frailties, where the frailty means follow either a Markov Random Field (MRF) or a stationary Gaussian Random Field (GRF) kriging model. They used a kind of hybrid Markov Chain Monte Carlo (MCMC) scheme, plugging in the Breslow estimator for the baseline hazard at each updating" step.Carlin and Banerjee (2002) and Banerjee and Carlin (2003) combined Markov Random Field and Gaussian Random Field priors for the spatial component with nonparametric estimation of the baseline hazard rate. Effects of continuous covariates are still assumed to be of linear parametric form.

Full and empirical Bayes inference in hazard regression models that can deal with all the afore-mentioned issues have been developed by Kneib and Fahrrmeir (2004) and Hennerfeind *et al* (2006).Bogaerts *et al* (2002) modeled interval censoring via data augmentation, frailties are used to incorporate correlations, transformation models for interval censored survival times in combination with a generalized estimating equations approach to account for correlations.Cai and Betensky (2003) presented a mixed model approach to estimate the baseline hazard rate in the presence of interval censoring based on penalized splines. Their model also allows for the inclusion of parametric covariate effects.

2.0 Methodology

We examine variations in malnutrition prevalence asit relates to household socio-economic factors, contained in Multiple Indicators Cluster Survey-3 (MICS3) data, including spatial variation in under-five malnutritionwith flexible geo-additive semi-parametric mixedmodel, while simultaneously controlling for spatialdependence and possibly nonlinear effects of covariateswithin a simultaneous, coherent regression framework. Because the predictor contains usual linearterms, nonlinear effects of metrical covariates and geographiceffects in additive form, such models are alsocalled geo-additive models. Kammann and Wand (2003), proposedthis type of models within an empirical Bayesianapproach. Here, we apply a fully Bayesian approach assuggested in (Fahrmeir and Lang, 2001) which is based on Markov priors anduses Markov Chain Monte Carlo (MCMC) techniquesfor inference and model checking, itroutinely used the Deviance Information Criterion (DIC)developed in Spiegelhalter *et al* (2002), as a measure of fitand model complexity.

The analysis was carried out using BayesX software package, which permits Bayesianinference based on MCMC simulation techniques. Thestatistical significance of apparent associations betweenpotential risk factors and the wasting malnutrition components was used to evaluate the significance ofthe posterior mean determined for the fixed effects or the categorical data, while non-lineareffects and spatial effects were analysed using the estimation of spatial effects based on Markov random fields, stationary Gaussian random fields, and two-dimensional extensions of penalized splinesproperties of the programme and viewing the map through GSview 4.9 software. We also run a sensitivity analysis for the choice ofpriors. Standard choices for the hyper-parameters are a = b = 0:001, with 25000 iteration and burn-in period of 5000, there are 17093 observations.

3.0 The Models

Kneib(2005), considered Cox-type hazard rate models

$$\lambda_i(t) = \exp(\eta_i(t)), \qquad \text{...(3.1)}$$

where

$$\eta_i(t) = v_i'\gamma + g_0(t) + \sum_{l=1}^{L} g_l(t)u_{il} + \sum_{j=1}^{J} f_j(x_{ij}) + f_{spat}(S_i) + b_{gi} \qquad \text{...(3.2)}$$

and

$$f_{spat}(S_i) = f^{str}{}_{(spat)} + f^{unstr}{}_{(spat)} \qquad \text{...(3.3)}$$

Here $g_0(t) = \log(\lambda_0(t))$ is the log-baseline effect, $g_l(t)$ are time-varying effects of covariates u_{il}, f_j are nonlinear effects of the continuous covariates x_{ij}, $f_{spat}(s_i)$ is a spatial (structured and unstructured) effect, and γ is the vector of usual linear fixed effects, and b_g is a subject or group specific frailty or random effect, with $b_{gi} = b_g$ if individual I is in group g, where g = 1, . . ., G and G = n, we obtain individual-specific frailties, for G < n.Under the usual assumption about non informative censoring, the Likelihood is given by

$$L = \prod_{i=1}^{n} \lambda_i(t_i)^{\delta_i}.\exp\left(-\int_0^{t_i} \lambda_i(u)du\right) = \prod_{i=1}^{n} \lambda_i(t_i)^{\delta_i}.s_i(t_i) \qquad \text{...(3.4)}$$

To ease the description of inferential details and to obtain a compact formulation of structured hazard regression models, we introduce some matrix notation. All different effects in (3.2) can be cast into one general form and each vector of function evaluations can be written as the product of a design vector $v_{ij}(t)$ and a possibly high-dimensional vector of regression coefficients ξ_j.

For defining priors and developing posterior analysis the observation model (3.1) is rewritten in generic matrix notation. Let $\eta = (\eta_1, \ldots, \eta_i, \ldots, \eta_n)'$ denote the predictor vector, where $\eta_i := \eta_i(t_i)$ is the value of predictor (3.4) at the observed lifetime t_i, $i = 1, \ldots, n$. Correspondingly, let $g_l = (g_j(t_1), \ldots, g_l(t_n))'$ denote the vector of evaluations of the functions $g_l(t)$, $l = 0, \ldots, L$, $f_j = (f_j(x_{1j}), \ldots, f_j(x_{nj}))'$ the vector of evaluations of the functions $f_j(x_j)$, $j = 1, \ldots, J$, $f_{spat} = (f_{spat}(s_1), \ldots, f_{spat}(s_n))'$ the vector of spatial effects, and $b = (b_{g1}, \ldots, b_{gn})'$ the vector of uncorrelated random effects. Furthermore, let $\bar{g}_l = (g_l(t_1)u_{1l}, \ldots, g_l(t_n)u_{nl})'$, l= 1, . . ., L. Then the vectors g_0, $\bar{g}_l$, f_j, f_{spat} and b can always be expressed as the matrix product of an appropriately defined design matrix v_{ij}, and a (possibly high-dimensional) vector ξ_j of parameters, e.g. $\bar{g}_l = v_{ij}\xi_l$, $f_j = v_{ij}\xi_j$, and so on. This also applies to the time-varying effects and, hence, after appropriate reindexing and suppressing the time index, the predictor (3.2), we can represent the predictor vector η in generic notation as

$$\eta_i = u_i'\gamma + v_{i1}'\xi_1 + \ldots + v_{ip}'\xi_p \qquad \ldots(3.5)$$

where $u_i'\gamma$ represents parametric effects while each of the terms $v_{ij}'\xi_l$ represents a non-parametric effect. Defining stacked vectors and matrices $\eta = (\eta_i)$, $U = (u_i)$, $V_j = (v_{ij})$, it gives

$$\eta = U\gamma + V_1\xi_1 + \ldots + V_p\xi_p \qquad \ldots(3.6)$$

3.1 Gaussian Processes: It has been shown that many Bayesian regression models based on neural networks converge to Gaussian processes in the limit of an infinite network (Neal 1996). This has motivated examination of Gaussian process models for the high-dimensional applications to which neural networks are typically applied (Williams and Rasmussen 1996). The empirical work of Rasmussen (1996) has demonstrated that Gaussian process models have better predictive performance than several other nonparametric regression methods over a range of tasks with varying characteristics. The conceptual simplicity, flexibility, and good performance of Gaussian process models make them very attractive for a wide range of problems. Hence, the process was modified to fit into the Generalized Additive Mixed Model (GAMM) of Bayesian method. Furthermore, the response variables of interest are defined for Gaussian process as:

$$y \sim N(\mu, \Sigma), \text{ and } y \sim f(\gamma),$$
$$\text{where } \gamma = \beta_o + \beta_i X_i + \ldots + \beta_k X_k + f(Z)$$

Where yis the regression response for wasting with respect to Gaussian regressions. Andγ is the geoadditive predictor which can be specified for a particular child *i.* The β_0, $\beta_i X_i$ and f(Z)represent the estimates of the unknown nonlinear smoothing effects of the metrical covariates child's age (cage), a vector of the fixed effect parameters and the spatial effect respectively. To enhance identifiability, functions are centred about zero, thus the fixed effect parameters automatically include an intercept term γ_0.

Wasting = WHZ (Normal regression)

where:WHZ – Weight for Height Z-score use to measure Wasting

3.2 Binomial regression: Ibrahim and Laud (1991) considered the Jeffreys prior for β in a GLM, giving special attention to its use with logistic regression. They showed that it is a proper prior and that all joint moments are finite, as is also true for the posterior distribution. Daniels and Gatsonis (1999) used such modeling to analyze geographic and temporal trends with clustered longitudinal binary data. Biggeri *et al* (2004) used it to investigate the joint contribution of individual and aggregate (population-based) socioeconomic factors to mortality in Florence. They illustrated how an individual-level analysis that ignored the multilevel structure could produce biased results.Hence, the need to consider the multilevel analysis as against the individual level analysis used with the Gaussian process, therefore the Binary regression was modified to fit into the Generalized Additive Mixed Model (GAMM) of Bayesian method. Also, the response variables of interest are defined for Binomial process as:

$$y \sim B(n, p) \text{ and } y \sim f(\eta),$$
$$\text{where } \eta = f(cage_i) + f_{spat}(s_i) + v_i'\gamma$$

Where yis the regression response for wasting with respect to Binomial regressions. And where ηis the geoadditive predictor which can be specified for a particular child *i.* The $f(cage_i)$, $f_{spat}(s_i)$ and γrepresent the estimates of the unknown nonlinear smoothing effects of the metrical covariates cage(child's age), the spatial effect and a vector of the fixed effect parameters. To enhance identifiability, functions are centred about zero, thus the fixed effect parameters automatically include an intercept term γ_0.

$$\text{wastbin} = \begin{cases} 1 & \text{if WHZ} < -2 \\ 0 & \text{otherwise} \end{cases} \qquad \text{---- binary regression}$$

4.0 Results and Discussions

Nigerian children nutritional data was analyzed with the aim of assessing the influence of some covariates on the response variable (wasting). Since the Multiple Indicator Cluster Survey3 (MICS3) data set contains several variables, only those that are believed to be related to nutritional status were selected. All categorical covariates are effect coded. The child's age is assumed to be nonlinear; the state is spatial effect while other variables are parametric in nature.Based on the anthropometric index of weight-for-height of children under five (years) measured as z-scores (that is the standard deviations from the median of the reference population) such that

$$z_i = \frac{WHi - Med}{s.d}$$

Where WH_i is the anthropometric index of weight-for-height for a child i, Med and s.d. are the median and the standard deviation of the reference population respectively.The variables are defined as follows:

Area: Sector
- Rural (reference location)
- Urban

Geopolitical Zones
- NC – North Central (reference zone)
- NE – North East
- NW – North West
- SE – South East
- SS - South South
- SW – South West

Mother's Education
- None (reference educational level)
- Primary
- Secondary
- Non-Standard Curriculum (non-std)

Parents' Wealth Index Quintiles
- Poorest (reference wealth index)
- Windex2 – Second rich
- Windex3 – Middle rich
- Windex4 – Fourth rich
- Windex5 – Richest

Sex:
- Female (reference sex)
- Male

4.1 Wasting Gaussian Regression

```
>f.regress wasting =state_rec(spatial, map=m, lambda=0.1) + CAGE(psplinerw2) + urban + WIndex2 + WIndex3 + WIndex4 + WIndex5 + primary + secondary + non_stdcur + UF11 + male + NEast + NWest + SEast + SSouth + SWest, iterations=25000 burnin=5000 step=20 family=gaussian predict using d
```

4.2 Wasting Binomial Regression

```
>f.regress wastbin = state_rec(spatial, map=m, lambda=0.1) + CAGE(psplinerw2) + urban + WIndex2 + WIndex3 + WIndex4 + WIndex5 + primary + secondary + non_stdcur + UF11 + male + NEast + NWest + SEast + SSouth + SWest, iterations=25000 burnin=5000 step=20 family=binomial predict using d
```

Table 1- Wasting: Gaussian and Binomial Regression Analysis

Variable	**Gaussian** Odds ratio	95% Confidence Interval lower limit	upper limit	**Binomial** Odds ratio	95% Confidence Interval lower limit	upper limit
Urban	1.1555	1.0366	1.2959	0.7366	0.0575	0.1951
Wealth Index2	0.8971	0.7955	1.0101	1.1238	0.6176	0.8737
Wealth Index3	0.8873	0.7763	1.0199	1.1020	0.9487	1.3251
Wealth Index4	0.9940	0.8587	1.1497	0.9765	0.8978	1.3329
Wealth Index5	0.9685	0.8156	1.1537	0.9832	0.7675	1.2273
Primary	1.0453	0.9422	1.1671	0.9100	0.7388	1.2865
Secondary	1.0492	0.9190	1.1862	0.8841	0.7593	1.0933
Non-std. curriculum	0.9810	0.7326	1.3153	0.7480	0.7206	1.0901
Male	0.8729	0.8075	0.9398	1.1311	0.4685	1.1395
Northeast	0.8081	0.6098	1.0433	0.8928	1.0043	1.2831
Northwest	0.9480	0.5869	1.4454	0.8903	0.6254	1.3168
Southeast	1.1134	0.6637	1.9255	0.9780	0.5102	1.6003
Southsouth	1.0010	0.5918	1.8291	0.6095	0.5244	1.8865
Southwest	1.4385	0.8350	2.7464	0.7023	0.3155	1.1918

The above table shows that at 95% Confidence Interval, the prevalence of moderately wasting (Gaussian) was higher among children living in the urban area with 15%more than their counterpart in the rural area, as observed by Emina *et al* (2011), with reference to the province of residence, children living in Kinshasa are less likely to suffer from stunting, they are more likely to experience wasting compared to their counterpart living in other provinces. While severe wasting (Binomial) was about 26%lower in children living in urban area. When comparing the two situations, we discovered that wasting which is usually the result of a recent nutritional deficiency is prevalence in children living in rural area than their counterpart in the urban region.

Wealth of the parents were positively associated with moderate wasting of under five children (Gaussian) because children from the richest parents have about 3%less chance of wasted, the children from fourth, middle and second rich parent have 1%, 11% and 10%less of wasted than their counterpart from poor parents. Also, the richer the parents the less severely wasted (Binomial) the child, as the richest and the fourth rich parents has 2%less severely wasted children each, the middle 10%more and the second rich parents with 11%more of severely stunted children. Hence, severe wasted children are prevalence with rich parents as observed by Kandala *et al* (2011) that, the association between maternal education and wasting is not significant after accounting for socioeconomic characteristics.

Mother education inversely influence the moderate wasting (Gaussian) status of their children, as children from mothers with primary and secondary education have 5%more of wasted children each than the parents with no education, and the children from mothers with non-standard curriculum have 2%less chance of wasted children compared with children from mothers with no education. This was also observed by Emina *et al* (2011) that there is positive association between maternal education and the likelihood of being wasted only, compared to children whose mothers have no education or have attended only primary school, children of the most educated mothers experienced a high risk of being wasted only: 6.6% of the children whose mothers have secondary education or higher were wasted only, about 40% more than children whose mothers have no education or attended only primary school (4.7%).

On the other hand, mother education has positive effect on severely wasted children, as mother with secondary education and above has 12%less of severely stunted children, 9%less for mothers with primary education and 25%less for mothers with non-standard curriculum than children from non-educated mothers. This express the findings of Kandala et al (2011) that children of the most educated women are more likely to experience wasting than their counterparts in the DRC.

Male children are 13%less moderately wasted (Gaussian) than their female counterpart, while they (male) are 13%more severely wasted than female. On the regional effect, the northern regions have less prevalence of moderate wasted (Gaussian) children with North East and North West having 19% and 5% less respectively compared with the North Central, while the Southern regions have more prevalence of moderate wasted children with South East and South West having 11%, and 43% more respectively, with South-South having almost equal chance of moderate wasted children when compared with the North Central.

On the other hand, the prevalence of severe wasted (Binomial) is less pronounced in any of the region as the North East and North West were having 11%less each, South East, South-south and South West were having 2%, 39% and 30%less of severe wasted children compared with the North Central. It can be deduced that South-south and South West have significant less chance of severe wasted children

The nonlinear effect of child's age in the Wasting Gaussian processis displayed in Figure 1a. The graph shows that the nutritional status of the child followed an irregular pattern, although there is a linear tendency in the graph which can be interpreted that a child wasted status is fair from birth till about after 3years of life when it start fluctuating. In Figure 1b, the colour white is associated with positively significant states, the colour black with negatively significant states, and the colour grey with non-significant states. The posterior means within 95% credible interval showing that only Lagos state have positively significant wasted children, while Borno, Kano, Kaduna, Bauchi and Adamawa states having less wasted children, with the remaining states are not statistically significant in children with wasting.The child's age graph (figure 2a) shows an irregular pattern as the severely wasted children improves as they grow from birth to after one year of life and falls around two years in life only to start picking up again after four years of life. The state effect (figure 2b) shows that only Zanfara and Benue have positively significant effect, which implies that they have more severely wasted children, while Kebbi, Jigawa, Plateau and Borno states have negatively significant severely wasted effect, with other states having statistically non-significant effect of severely wasted children.

5.0 Conclusion

The aim of site-specific province analysis is to accelerate policy interventions, optimise inputs (unobserved factors such as distal ones: food security and prices policies, environmental), improve child nutrition by taking into account the environmental impact and reduce the timescale to attain the Millennium Development Goals (MDGs). It is an approach that deals with multiple groups of factors input to improve child nutritional status in order to satisfy the actual needs of parts of the provinces rather than average needs of the whole country.In comparing the Gaussian and Binomial analysis, one important thing to note is that, Gaussian regression analyses assume a normally distributed data, the properties of a normal distribution holds. This implies that the Gaussian analysis result is for moderate or global nutritional deficiency status, while the Binomial analysis result is for severe cases of nutritional deficiency. Hence, the only condition for comparison is to see which of the determinants is moderate or severe with respect to which of the factors. For this reason, it means that the bases of their comparison would not be to infer that one method of the analysis is more suitable than the other, since the parameters are assessed with different perspectives.

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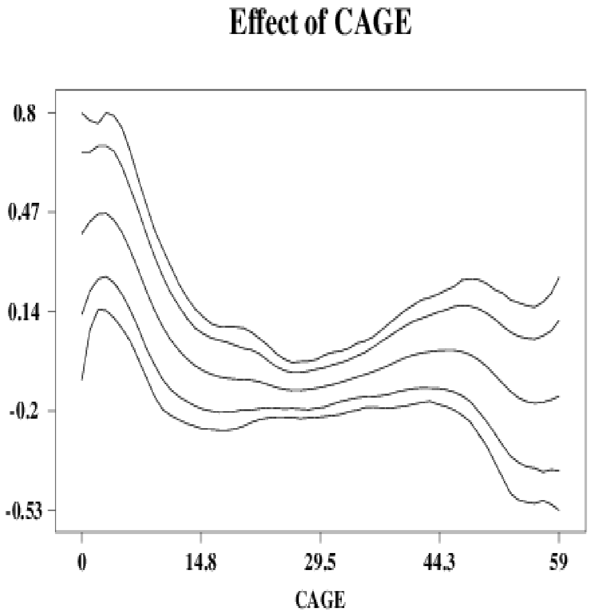
FIGURES



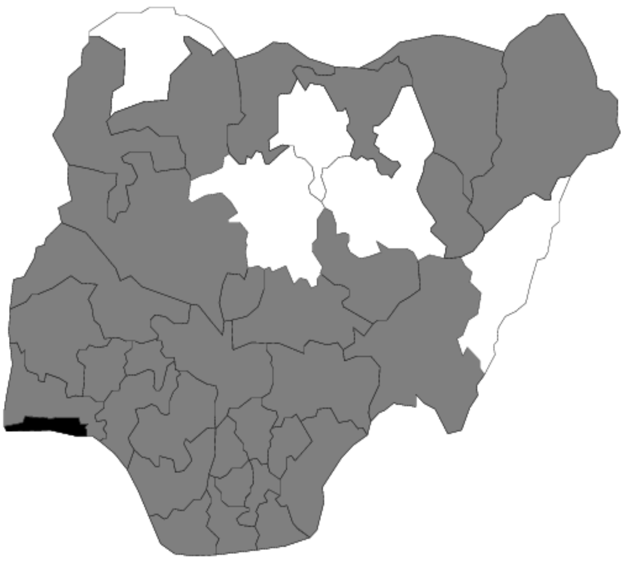
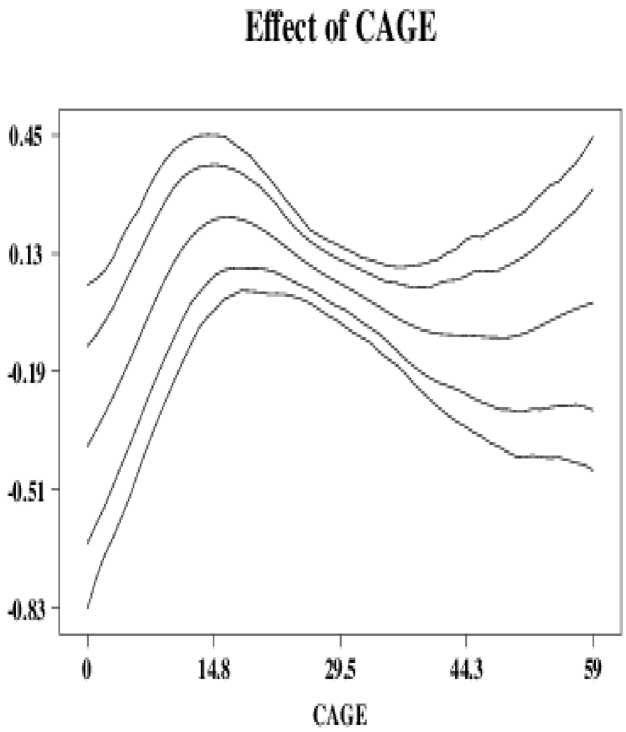


Fig.1a: Effects of Child Age (in months) on Wasting (Gaussian Analysis)

Fig.1b: State Effect on Wasting (Gaussian Analysis) at 95% CI



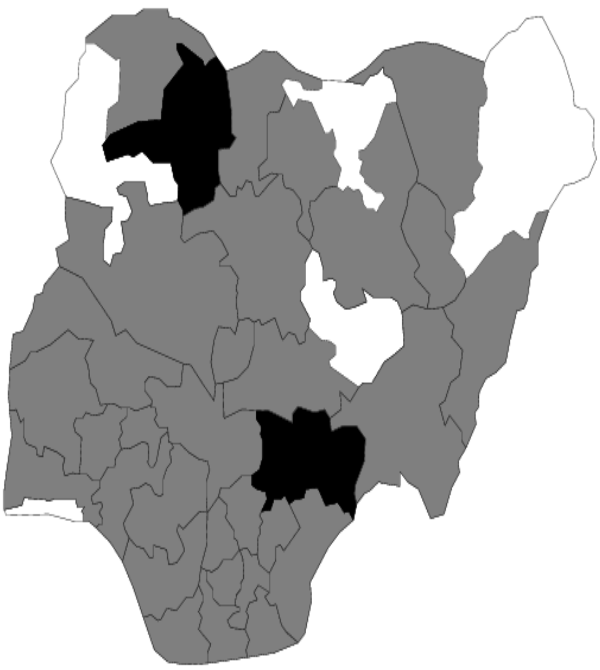


Fig.2a: Effects of Child Age (in months) on Wasting (Binomial Analysis)

Fig.2b: State Effect on Wasting (Binomial Analysis) at 95% CI