# An Alternative Stratified Cox Model for Correlated Variables in Infant Mortality

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**Abstract:** Often in epidemiological research, introducing a stratified Cox model can account for the existence of interactions of some inherent factors with some major/noticeable factors. This paper aims at modelling correlated variables in infant mortality with the existence of some inherent factors affecting the infant survival function. A Stratified Cox model is proposed with a view to taking care of multi-factor-level that has interactions with others. This, however, is used as a tool to model infant mortality data from Nigeria Demographic and Health Survey (NDHS) with g-level-factor (Tetanus, Polio and Breastfeeding) having correlations with main factors (Sex, infant Size and Mode of Delivery). Asymptotic properties of partial likelihood estimators of regression parameters are also studied via simulation. The proposed models are tested via data and it shows good fit and performs differently depending on the levels of the interaction of the strata variable Z*. An evidence that the baseline hazard functions and regression coefficients are not the same from stratum to stratum provides a gain in information as against the usage of the Cox model. Simulation result shows that the present method produces better estimates in terms of bias, lower standard errors, and or mean square errors.

**Keywords:** Stratified Cox, Semiparametric model, infant mortality, multifactor-level, confounding variables.

## 1. INTRODUCTION

The extension of Cox Proportional Hazard Model (PHM) [1] addresses the failure of proportionality assumption by the introduction of time dependence covariate (Internal/External). Often times, the prognostic factors at different level produce hazard function that differs markedly from proportionality in the presence of Time-Dependent (TD) in relative risk, and this may not be of interest. Stratification on these factors provides a simpler and better approach.

Consider a continuous survival time variable $T,(T \geq 0)$ and fixed covariates $X^{(1)}, X^{(2)}, X^{(3)}, \cdots, X^{(n)}$ which are row vectors of dimension $p^{(1)}, p^{(2)}, \ldots, p^{(n)}$ respectively. To assess the effect of $X^{(1)}$ on T, holding $X^{(2)}, X^{(3)}, \cdots, X^{(n)}$ as a confounding variables, we will want to apply Cox PHM [1],

$$h(t:x) = h_o(t)\phi(t;x), \qquad t > 0 \tag{1}$$

where $\phi(t;x) = \exp(X'\beta)$

Model (1) assumes that for any two covariates set $\{X^{(1)}, X^{(2)}\}$ the hazard satisfies,

$$h(t:X^{(1)}) \propto h(t:X^{(2)}), \qquad t>0 \tag{2}$$

Suppose that there exists another covariate $X^{(3)}$ which failed the proportional hazards assumption, then it is possible to split $X^{(3)}$ into subgroups of homogeneous strata represented by g-level-factor. A modification of (1) by stratification of such covariate(s) is included in the model; whereas the factor being stratified is not included, Ata and Zozer [2]. Arasan and Lunn [3], extended the bivariate model of Freund [4] to incorporate time-varying covariate as a result of the failure of Proportional Hazard Assumption (PHA) of fixed covariates over time as against the current values of covariates which may be more meaningful. The concept of information gained to measure both global and partial dependence between explanatory variables and a censored response within the framework of PHM were extended to investigate stratified Cox model by Heinzl et:al [5]. Zhang et:al [6], directly adjusted survival curves for different treatment groups for a stratified Cox model. They however constructed the estimators by taking the average of the individual predicted survival curves using SAS macro. Zhang et:al [7], introduced a SAS macro that computes the restricted mean survival times from directly adjusted survivals based on stratified Cox model. Pennells et:al [8], introduced some measures to assess the prognostic ability of the stratified Cox PHM. They chose three measures developed for the unstratified Cox Proportional Hazards (CPH) model, adapted them for use with the stratified CPH model and demonstrated how their values could be represented over time.

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Dupuy and Leconte [9], studied the appropriateness of regression calibration method in partially observed stratified Cox model with missing values of the covariate defining the strata. An efficient and alternative method of stratified Cox model was investigated by Mehrotra et:al [10]. The major aim of this work is to examine the correlation that exists within each level (stratum) of the model which in principle usually causes bias and affect variances and mean square error of the parameter estimates.

## 2. STRATIFIED COX MODEL

Classical Stratified Cox Model

Suppose there are g strata created on the stratification variable X, then, a classical stratified Cox PHM accommodates distinct baseline hazard functions ($h_o^j(t); j = 1, 2, \cdots, g$) for each stratum but enforces a common relative risk factor or ratio across strata. We define the hazard function for an individual in the j[th] stratum (level) as

$$h_j(t : x) = h^j{}_o(t)\phi(Z(t)'\beta), \qquad j = 1, \cdots, g \qquad t > 0 \quad (3)$$

where Z(t) is the $X\left(X^{(1)}, X^{(2)}, \cdots, X^{(p)}\right)$; $Y\left(Y^{(1)}, Y^{(2)}, \cdots, Y^{(k\ 1)}\right)$ vector of covariates, Kleinbaum [11].

Multifactor-level Stratified Cox Model

Suppose $X\left(X^{(1)}, X^{(2)}, \cdots, X^{(p)}\right)$ satisfy and $Y\left(Y^{(1)}(t), Y^{(2)}(t), \cdots, Y^{(k\ 1)}(t)\right)$ do not satisfy PHA. Let m-factor-level variables failed, then, the variables can be stratified into g strata according to the variable that failed the assumption. From (3), we defined a multifactor-level stratified Cox model as:

$$h_j(tjx) = h_0{}^j(t)\exp\left[\begin{pmatrix}\beta_1 X^1 + \cdots + \beta_p X^p + \beta_{11}\left(Y^1 X^1\right) + \cdots \\ + \beta_{1p}\left(Y^1 X^p\right) + \cdots + \beta_{(k\ 1)p}\left(Y^{k\ 1} X^p\right)\end{pmatrix}\right] \quad (4)$$

$j = 1, \cdots, g$ strata from $Y$, $i = 1, \cdots, p; t > 0.$

where $\beta_{ij}$ is the coefficient of the interactions between j[th] variable of X and i[th] variable of Z confounding variables. The baseline hazard function for the g strata are allowed to be arbitrary and assumed completely unrelated. We use approximate partial likelihood of $\beta$ which is the product of terms

$$L(\beta) = \prod_j^g h_j(t_j \mid x_j)^{\delta_j} S_j(t_j \mid x_j) \quad (5)$$

which is the partial likelihood of $\beta$ arising from the j[th] stratum alone. Maximizing (5) using Newton-Raphson technique generally leads to quick convergence in the estimate of $\beta$. A crucial feature of model (3) is its invariance under differentiable, strictly monotonic increasing transformations acting on time scale in each stratum, Kalbfleisch [12].

## 3. SIMULATION STUDY

We performed simulation study based on model (3) and (4) and observed a situation that accounted for cofounder variables by stratification. Let T be the failure time and three covariates of which one is time fixed (X) and other factors are time varying covariates $Z(Z^{(1)}; Z^{(2)})$ each at two levels $Z_1{}^{(1)}$ and $Z_2{}^{(1)}$, $Z_1{}^{(2)}$ and $Z_2{}^{(2)}$. X was generated from N(0,1), while $Z^{(1)} \sim U(0; 1)$ and $Z^{(2)} \sim$ bin(n, p=0.5) distributions. We chose the initial regression coefficients as follows: $\beta_1 = 1$; $\beta_{11} =$ log(1.25); $\beta_{12} =$ log(0.25) and $\beta_{13} = 2.5$. Four different sample sizes were considered n= (20, 50, 100 and 500) and replicated 10,000 times to obtain empirical distributions of the estimators of parameters using R-program.

## 4. RESULTS FROM SIMULATION STUDY

Results for classical model (3) and multifactor-level model (4) are presented in Tables **1** and **2**. In these tables the sample size, parameter estimates, bias, absolute bias, variance and mean square error (MSE) are given. Estimates from the classical stratified cox model are presented in Table **1** and these are as depicted in Figure **1**. Asymptotically, the plots of variance and MSE indicated that the higher the sample size the lower the values of absolute bias, variance and MSE.

In Table **2**, the results of simulation obtained from model with interaction are as presented. From the results, the estimated mean, absolute bias, variance and MSE, for multifactor-level model are given for all the parameters (including the interaction parameters $\beta_{11}$; $\beta_{12}$; and $\beta_{13}$). The estimates are highly statistically consistent. Figures **2** and **3** depict estimated variance and estimated MSE respectively.

Figures **4** and **5** show the plots of the estimates from classical stratified Cox model and multifactor-level with interactions. In Figure **4**, comparison of absolute bias values of both stratified Cox (3) and multifactor-

**Table 1: Simulation Study with Various Sample Sizes for Model (3)**

| Sample size | $\hat{\beta}$ | Bias( $\hat{\beta}$ ) | Absolute Bias( $\hat{\beta}$ ) | Var( $\hat{\beta}$ ) | MSE( $\hat{\beta}$ ) |
|---|---|---|---|---|---|
| 20 | -0.264 | -1.264 | 1.264 | 2.761 | 4.359 |
| 50 | -0.040 | -1.040 | 1.040 | 0.275 | 1.357 |
| 100 | 0.055 | -0.945 | 0.945 | 0.105 | 0.998 |
| 500 | 0.145 | -0.855 | 0.855 | 0.016 | 0.747 |

**Table 2: Simulation Study with Various Sample Sizes for Model (4)**

| Sample size | $\hat{\beta}_1$ | $\hat{\beta}_{11}$ | $\hat{\beta}_{12}$ | $\hat{\beta}_{13}$ |
|---|---|---|---|---|
| 20 | 0.083 | -0.917 | 0.273 | 1.114 |
| 50 | 0.108 | -0.115 | 0.372 | 0.385 |
| 100 | 0.216 | 2.113 | 1.063 | 5.529 |
| 500 | 0.058 | -2.443 | 0.687 | 6.652 |
| /Bias | $B_1$ | $^{B}11$ | $^{B}12$ | $^{B}13$ |
| 20 | 0.125 | 0.081 | 0.096 | 0.094 |
| 50 | -0.875 | -0.143 | 1.993 | -2.406 |
| 100 | 0.156 | 0.217 | 0.517 | 0.363 |
| 500 | 0.922 | 0.237 | 4.490 | 6.151 |
| Absolute Bias | $AB_1$ | $AB_{11}$ | $AB_{12}$ | $AB_{13}$ |
| 20 | 0.125 | 0.080 | 0.096 | 0.094 |
| 50 | 0.875 | 0.143 | 1.993 | 2.406 |
| 100 | 0.156 | 0.217 | 0.517 | 0.363 |
| 500 | 0.922 | 0.237 | 4.490 | 6.151 |
| Variance | Var( $\hat{\beta}_1$ ) | Var( $\hat{\beta}_{11}$ ) | Var( $\hat{\beta}_{12}$ ) | Var( $\hat{\beta}_{13}$ ) |
| 20 | 0.156 | 0.071 | 0.029 | 0.076 |
| 50 | 0.843 | 0.152 | 1.926 | 2.424 |
| 100 | 0.107 | 0.153 | 0.372 | 0.264 |
| 500 | 0.819 | 0.177 | 4.081 | 6.138 |
| MSE | Mse( $\hat{\beta}_1$ ) | Mse( $\hat{\beta}_{11}$ ) | Mse( $\hat{\beta}_{12}$ ) | Mse( $\hat{\beta}_{13}$ ) |
| 20 | 0.172 | 0.078 | 0.019 | 0.087 |
| 50 | 1.609 | 0.172 | 1.916 | 2.414 |
| 100 | 0.131 | 0.123 | 0.289 | 0.186 |
| 500 | 1.668 | 0.143 | 3.960 | 6.010 |

level with interactions (4) models are depicted. Estimates from interaction model (4) give the least absolute biased values across all sample sizes; invariably, the estimates are asymptotically biased. Meanwhile, variances of estimates from classical stratified model give the least values. The values of MSE of estimates are shown in Table **2** give the least as sample size increases. Multifactor-level model provides the minimum variance and MSE relative to sample sizes. This contributes the fact that interaction model provides the best estimate with little or no bias and minimum MSE (see Figures **4** and **5**).

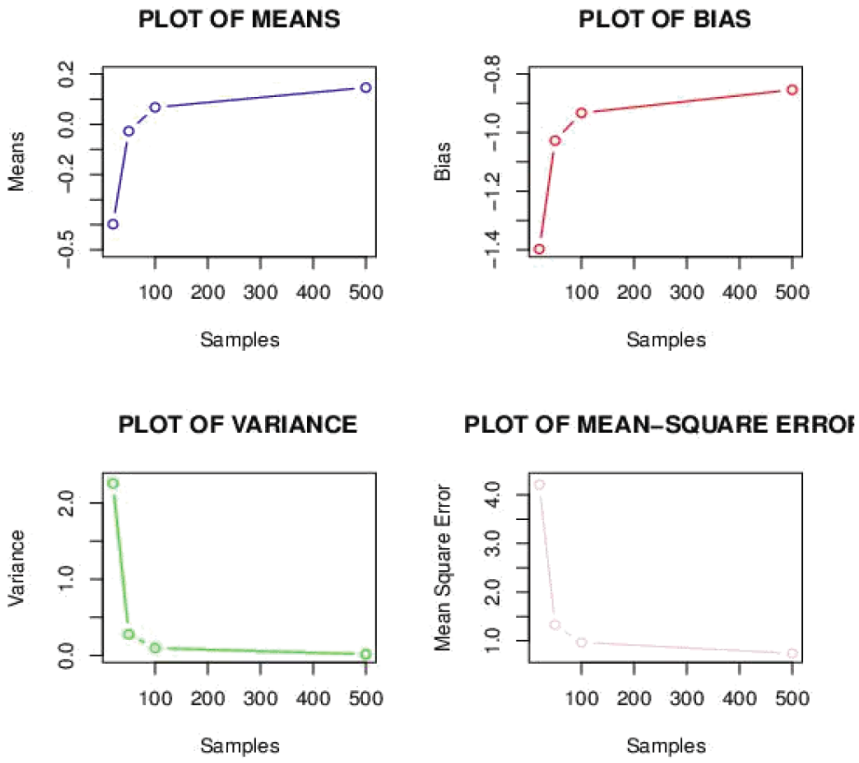


**Figure 1:** The plot of the distribution of estimates with sample sizes.

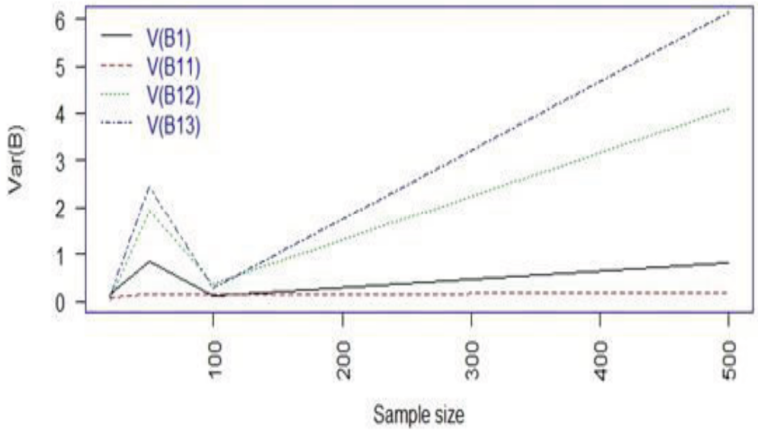


**Figure 2:** Plot of the estimated variances from multifactor-level model.

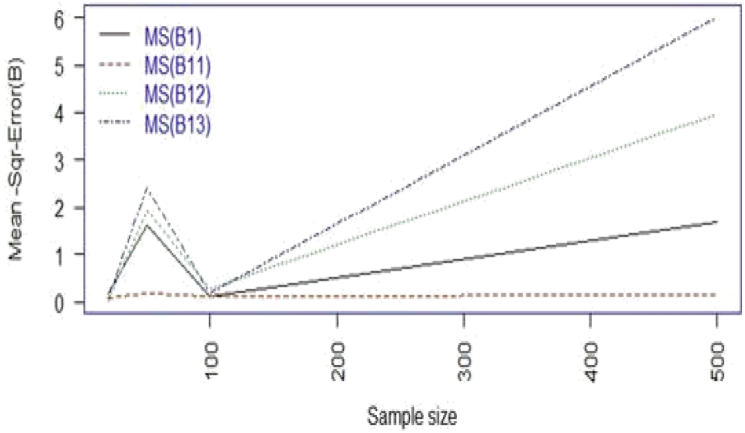


**Figure 3:** The plot of Mean Square Error from multifactor-level model.

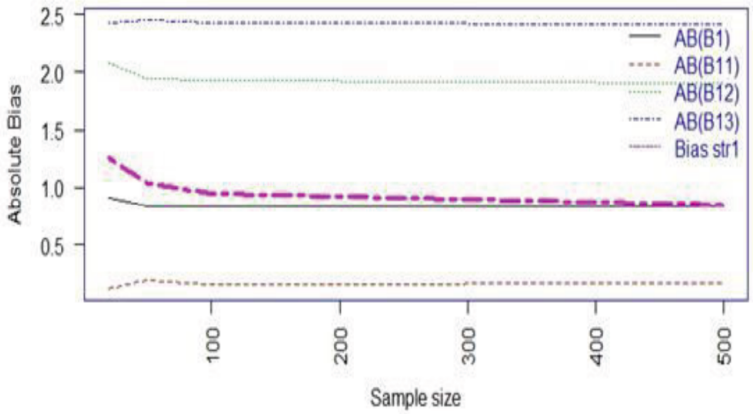


**Figure 4:** Comparison of Absolute Bias Estimates from Classical Stratified Cox and multifactor-level Stratified Cox with interaction models.

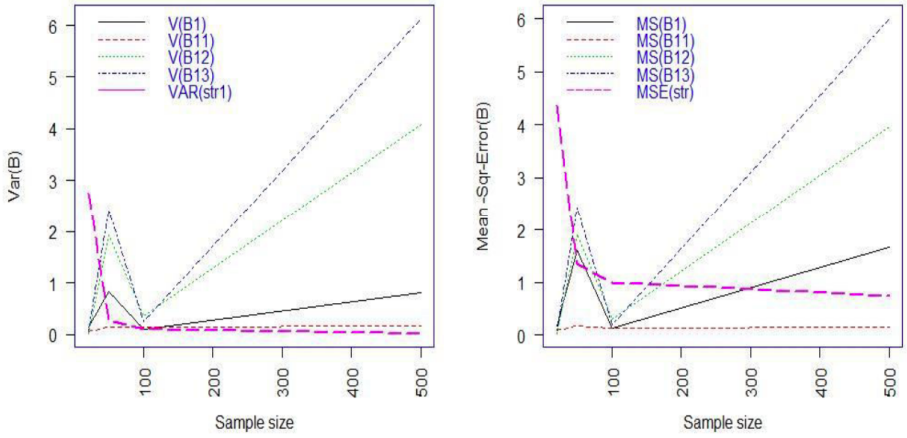


**Figure 5:** Comparison of Estimates from Classical Stratified Cox and multifactor-level Stratified Cox with interaction model.

## 5. APPLICATION

To illustrate the suitability of using these models, we applied both Cox PH, Stratified Cox (no interaction and interaction) models to data on infant mortality extracted from Nigeria Demographic Health Survey (NDHS) 2013. One of the goals of Millennium Development Goals is to reduce infant mortality rate from 64 to 30 deaths per 1000 live births by 2015,FRN [13]. The response variable is time to death of an infant (< 1 year old). This is measured as the time from birth to death before the first birthday. This study therefore looks critically into some factors which are thought to be associated with infant mortality and the ones collected for this study include: Sex, Tetanus treatment, Polio treatment, Infant size, Mode of delivery and Exclusive breastfeeding.

Let $\delta_i = 1$ (i= 1, …, n), if an infant died right before the first birthday at time $t_i$ and $\delta_i = 0$ if otherwise. Let the survival time $T = \min(t_i, C_i)$ where $C_i$ = 354 days, then

$$\delta_i = \begin{cases} 1, T_i \le C_i \\ 0, T_i > C_i \end{cases}$$

Table **3**, shows estimates from Cox regression model obtained from the infant mortality data using (1). First, we check the Schoenfeld residuals for proportionality assumption and discover that there exists correlation among the covariates (Tetanus, Polio and Breastfeeding) and time, (see Table **4**, Schoenfeld residual test). This shows strong evidence of nonproportionality of the variables and the model (1). As a result of this, model (1) is not appropriate for analyzing this data because some of the variables are time varying and the nature of the time cannot be ascertained [14]. Hence, there is high correlation between the covariates and time, see Table **4**. Fitting a stratified Cox model (3), we obtained the results displayed in Table **5**. From the result, tetanus treatment, polio treatment and breastfeeding were adjusted by stratification. Figure **6** shows the Kaplan-Meier survival curves of infant mortality for the year 2013. From the survival curves, we discover that the probability of infants surviving up to and including 8

months is 0.95 (95 % chances), and this probability drops to 0.90 (90% chances) at 10 months and subsequently 0.85 (85% chances) at 11 months. It shows that there is high probability of survivors of infants in the country for the year even at 11 months (85% chances). From Table **5**, we obtain the no interaction stratified stratum hazard functions given below. The major characteristic of this model is that the strata coefficients are the same but the baseline hazard functions are different.

$h_j(t : X; Z) = h_0^j(t)\exp[(b_1 sex + b_2 Size + b_3 Cs); j = 1; : : :; 6; t > 0$ (6)

$h_1(t : X) = h^1{}_0(t)\exp(0{:}047sex\ 0{:}004Size + 0{:}052Cs)$

$h_2(t : X) = h^2{}_0(t)\exp(0{:}047sex\ 0{:}004Size + 0{:}052Cs)$

$h_3(t : X) = h^3{}_0(t)\exp(0{:}047sex\ 0{:}004Size + 0{:}052Cs)$

$h_4(t : X) = h^4{}_0(t)\exp(0{:}047sex\ 0{:}004Size + 0{:}052Cs)$

$h_5(t : X) = h^5{}_0(t)\exp(0{:}047sex\ 0{:}004Size + 0{:}052Cs)$

$h_6(t : X) = h^6{}_0(t)\exp(0{:}047sex\ 0{:}004Size + 0{:}052Cs)$

From (4), an interaction model (7) is obtained, with three stratification variables (Tetanus, Polio treatments and Breastfeeding). The main effects are the first three variables (sex, infant size and mode of delivery (Cesarean session CS or Normal)). The next variables are product terms of interaction of 18 categories of strata variables $Z^*$ (Sex with six categories of $Z^*$, Infant Size with six categories of $Z^*$ and mode of delivery with six categories of $Z^*$). $Z^*$ consists of three binary (dummy) variables $(Z_1^*, Z_2^*, Z_3^*)$ for tetanus treatment, polio treatment and breastfeeding, where $Z_1^*$ =Tetanus, $Z_2^*$ =Polio and $Z_3^*$ = Breastfeeding.

$$Z_1^* = \text{Tetanus (T)} = \begin{cases} 1, \text{ received tetanus treatment} \\ 0, \text{ Not received} \end{cases}$$

$$Z_2^* = \text{Polio(P)} = \begin{cases} 1, \text{ received polio treatment} \\ 0, \text{ not received} \end{cases}$$

$$Z_3^* = \text{Breastfeeding(B)} = \begin{cases} 1, \text{ exclusively breastfeed} \\ 0, \text{ not exclusively breastfeed} \end{cases}$$

The matrix below represents the jth stratum by variables interactions (5).

$$\begin{pmatrix} 0 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ 1 & 1 & 0 \\ 1 & 0 & 1 \\ 0 & 1 & 1 \\ 1 & 1 & 1 \end{pmatrix}$$

$$\begin{aligned} h_j(t : X, Z^*) = h^j{}_o(t)\exp[&\beta_1 sex + \beta_2 Size + \beta_3 Cs + \beta_{11}(\text{sexT}) + \beta_{12}(\text{sexP}) + \beta_{13}(\text{sexB}) \\ &+ \beta_{14}(\text{sexTP}) + \beta_{15}(\text{sexTB}) + \beta_{16}(\text{sexPB}) + \beta_{21}(\text{sizeT}) + \beta_{22}(\text{sizeP}) \\ &+ \beta_{23}(\text{sizeB}) + \beta_{24}(\text{sizeTP}) + \beta_{25}(\text{sizeTB}) + \beta_{26}(\text{sizePB}) + \beta_{31}(\text{csT}) \\ &+ \beta_{32}(\text{csP}) + \beta_{33}(\text{csB}) + \beta_{34}(\text{csTP}) + \beta_{35}(\text{csTB}) + \beta_{36}(\text{csPB})]. \end{aligned} \quad (7)$$

The results of multilevel interaction model is as given below in Table **6**, and subsequently

$$\begin{aligned} j = 1 \quad & h_1(t : X, Z^*) = h_0^1(t)\exp[-0.005sex - 0.0026Size + 0.254Cs] \\ j = 2 \quad & h_2(t : X, Z^*) = h_0^2(t)\exp[0.0338sex - 0.4726Size - 0.427Cs] \\ j = 3 \quad & h_3(t : X, Z^*) = h_0^3(t)\exp[-0.04sex + 0.0314Size + 0.079Cs] \\ j = 4 \quad & h_4(t : X, Z^*) = h_0^4(t)\exp[0.006sex + 0.052Size - 0.41Cs] \\ j = 5 \quad & h_5(t : X, Z^*) = h_0^5(t)\exp[-0.025sex + 0.813Size - 0.132Cs] \\ j = 6 \quad & h_6(t : X, Z^*) = h_0^6(t)\exp[0.248sex - 0.0048Size - 0.372Cs] \\ j = 7 \quad & h_7(t : X, Z^*) = h_0^7(t)\exp[-0.408sex - 0.1086Size - 0.062Cs] \\ j = 8 \quad & h_8(t : X, Z^*) = h_0^8(t)\exp[-0.49sex - 0.0488Size - 0.0598Cs] \end{aligned} \quad (8)$$

the systems of equation.

From the multifactor-level interaction models above, there exists relationship/interaction between tetanus treatment, polio treatment, breastfeeding and the effect of infant sex, size and mode of delivery. This implies that the baseline hazard functions and regression coefficients are not the same from stratum to stratum. Also, some of the variables are highly associated with one another and this influences the hazards of infant mortality. In comparing the models, a log-likelihood ratio test is employed to compare the goodness of fit for the nested models. In all, the result of log-likelihood ratio statistics for multifactor-level interaction model (4) give the least of all relative to the classical stratified Cox model (3); (5755.013 < 5781.465).

## 6. CONCLUDING REMARKS

This study has brought out the beauty of correlation between the main factor and other stratification factors. It thus implies that there exists some factors affecting the process apart from the main noticeable factor(s) which are time fixed or time varying. Once the nature time varying cannot be actually understood or theoretically proved. This leads us to stratification. Although, Cox [1] model has become the most popular regression model for analyzing censored survival data both in medical and engineering research, as shown by many authors, stratified Cox model has helped in measuring the invariance to the quantity under independent censoring. It also helped to see how multi-factor-level are being used in stratified model and also affect the variability. Thoughtfully, situations in which the stratified Cox model could be used are quite common in practice, meanwhile, the actual use of the stratified Cox with interactions is much less frequent.

**Table 3: Estimates from Infant Mortality Data (Cox Regression Model 1)**

| | b | Se(b) | Z | Pr (> jzj) | Conf. Int(b) |
|---|---|---|---|---|---|
| Tetanus | 0.176 | 0.027 | 6.512 | 7.41e-11 | 1.131 - 1.257 |
| Polio | -0.486 | 0.027 | -17.825 | <0.001 | 0.583 - 0.650 |
| Breastfeeding | -0.051 | 0.004 | -11.584 | <0.001 | 0.942 - 0.958 |
| Sex | -0.016 | 0.025 | -0.675 | 0.500 | 0.937 - 1.032 |
| Size | 0.015 | 0.013 | 1.147 | 0.251 | 0.989 - 1.042 |
| Cs | 0.094 | 0.048 | 1.958 | 0.050 | 0.999 - 1.207 |

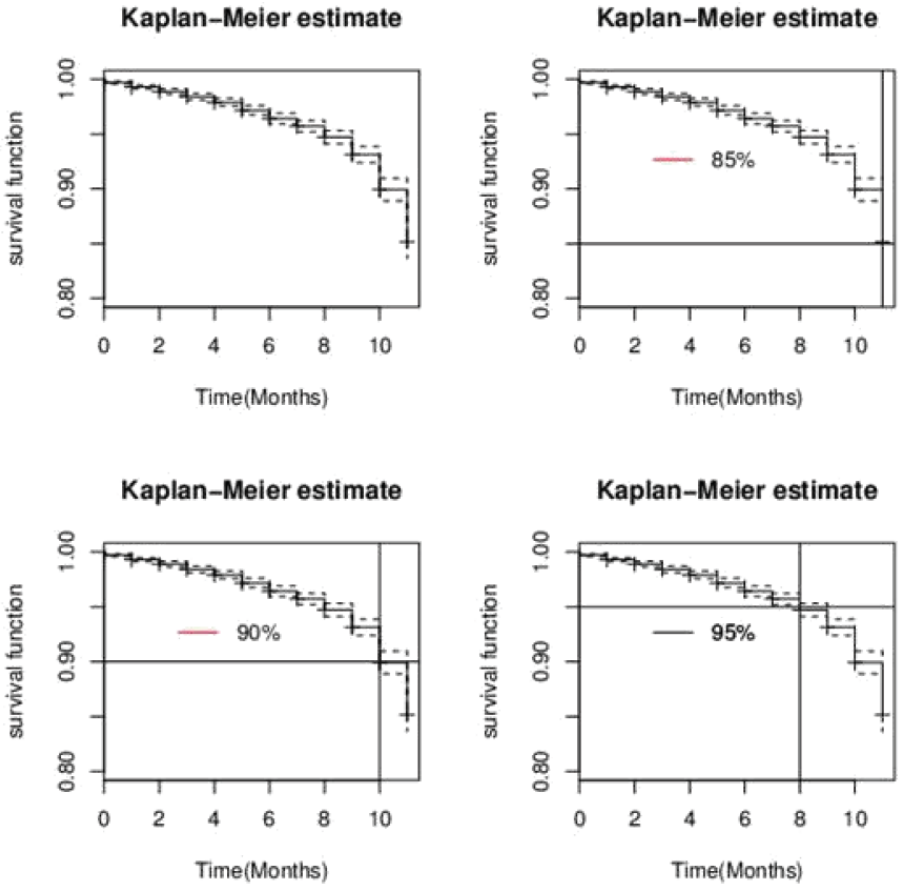


**Figure 6:** Plots of Kaplan Meier survivorship function for infant mortality data.

**Table 4: Schoenfeld Residual Test**

| | r | Chi-sq | Pr (> jzj) |
|---|---|---|---|
| Tetanus treatment | -0.037 | 9.445 | 0.002 |
| Polio treatment | 0.137 | 148.301 | < 0:001 |
| Breastfeeding | 0.117 | 2445.854 | < 0:001 |
| Sex | 0.010 | 0.691 | 0.406 |
| Size | -0.022 | 2.862 | 0.091 |
| Cs | 0.012 | 0.813 | 0.367 |
| Global | NA | 2745 | < 0:0001 |

**Table 5: Estimates from Infant Mortality Data (Stratified Cox Model 3)**

| | b | Se(b) | Z | Pr(> jzj) | Conf. Int(b) |
|---|---|---|---|---|---|
| Sex | -0.047 | 0.024 | -1.940 | 0.052 | 0.909 - 1.000 |
| Size | -0.004 | 0.0132 | -0.328 | 0.743 | 0.970 - 1.022 |
| Cs | 0.052 | 0.051 | 1.019 | 0.308 | 0.954 -1.163 |

**Table 6: Estimates from Multilevel Interaction Stratified Cox Model (4)**

| Variables | Coef( $\hat{\beta}$ ) | Se(Coef) | Z | Pr |
|---|---|---|---|---|
| Sex | -0.05 | 1666.28 | -3.00E-05 | 0.99 |
| Size | -0.0026 | 2970.91 | -8.75E-07 | 1 |
| Cs | 0.254 | 1.01 | 2.51E-01 | 0.042 |
| Sex*Tet | 0.06 | 2233.78 | 2.69E-05 | 1 |
| Sex*P | -0.056 | 1666.28 | -3.36E-05 | 0.99 |
| Sex*Tet*P | 0.082 | 2519.14 | 3.26E-05 | 1 |
| Sex*B | -0.31 | 1666.28 | -1.86E-04 | 0.037 |
| Sex*Tet*B | -0.172 | 3.87 | -4.44E-02 | 0.24 |
| Sex*P*B | 0.008 | 43.765 | 1.83E-04 | 0.019 |
| Cs*Tet | -0.681 | 3542.05 | -1.92E-04 | 1 |
| Cs*P | -0.175 | 2970.91 | -5.89E-05 | 1 |
| Cs*Tet*P | 0.152 | 2970.91 | 5.12E-05 | 0.12 |
| Cs*B | -0.014 | 31841.2 | -4.40E-07 | 0.059 |
| Cs*Tet*B | -0.131 | 67.085 | -1.95E-03 | 0.055 |
| Cs*P*B | -0.003 | 56.88 | -5.27E-05 | 0.45 |
| Size*Tet | -0.0388 | 1.44 | -2.69E-02 | 0.013 |
| Size*P | 0.034 | 1.02 | 3.33E-02 | 0.055 |
| Size*Tet*P | -0.112 | 1.29 | -8.68E-02 | 0.077 |
| Size*B | -0.174 | 1.67 | -1.04E-01 | 0.00344 |
| Size*Tet*B | 0.133 | 1.01 | 1.32E-01 | 0.0632 |
| Size*P*B | 0.034 | 1.54 | 2.21E-02 | 0.0556 |

These may be due to failure to thoroughly check the PH assumption or wrong application of the Cox model. So many other reasons might as well contribute to the usage of PH model.

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