

# **ESTIMATING MATERNAL OBSTETRIC RISK; THE APPLICATION OF SURVIVAL ANALYSIS TECHNIQUES**

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## **Abstract**

Studies on Maternal Survival and its converse mortality are of much recent origins with basic statistics, including data, in this area still a major challenge particularly for developing countries. While there are several estimators of maternal mortality and hence survival, the development of an appropriate measure of obstetric risk has been a challenge. In this study, the application of survival analysis techniques in developing appropriate estimates for maternal mortality and its usefulness have been proposed. Results of its application to data from Ghana showed that while about 92 % of pregnant women made it alive to delivery, only 83% of them survived to the end of the postpartum period. There were significant differentials by location, Obstetric history and Maternal Age: The Weibull distribution described maternal survival well.

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**Keywords:** Obstetric Risk, Maternal Mortality, hazard, Cohort, Survival Analysis, Maternal Survival

## **Introduction**

Improving maternal health is the fifth of the Millennium Development Goals. Motherhood is normally a positive and satisfying experience; yet many women suffer ill-health and even death in the process of attaining this fulfillment. Maternal health and mortality in particular, has devastating effect, not only on the mother, but also on the children left behind, her family, the society and nation as a whole (UNFPA, (2005); USAID, (2001); Reed, Koblinsky & Mosley, (2000)). Many studies in maternal mortality have been to provide up to date statistics of its state and also to see how close we are to achieving the millennium development goals. Some studies have also been to assess the impact of certain interventions in the reduction of these mortality levels. Some modelling have also been done in maternal survival, for the most part, to estimate Maternal Mortality Ratio

(MMRatio) in the absence of data, (Hakkert, (2001); Ahmed & Hill, (2011); Meda, Ouedraogo, & Ouedraogo, (2010)). Most of these studies have used linear models, and have basically been done to determine the extent to which some factors explain or influence MMRatio.

Special studies in developing countries in the 1980's, revealed a higher than anticipated number of maternal deaths; heightening interest in maternal mortality (WHO, 1991). These studies high-lighted the twofold problems of developing good and informative estimates of maternal mortality: The problem of availability of adequate and reliable data, and the problem of good statistical estimators. Many studies in maternal mortality, and its converse survival, have focused on ways to obtain better data (Graham, Ahmed, Stanton, Abou-Zahr, & Campbell, (2008); Chandromahan, Rodrigues, Muade, & Hayes, (1998); Boerma & Stansfield, (2007); Walker, Bryce, & Black, (2007); Graham & Hussein, (2006)) and neglected the need for good estimators. Progress made in data collection techniques and the competences of those engaged in the data collection process have increased the measurement opportunities of maternal mortality in developing countries in recent years (Graham, Brass, & Snow, 1989), (Stanton, et al., 2001), (Impact, 2007), (Amstrup, McDonald, & Manly, 2005). While much still needs to be done in this area, this study is focused on the problem of good statistical estimators.

Up till now, the estimates in use are largely central rates (i.e. Rates, Ratios, Probabilities etc.) with the three main indicators of maternal death being, Maternal Mortality Ratio (MMRatio), Maternal Mortality Rate (MMRate) and Lifetime Risk of maternal mortality (LR) as well as the use of the Proportion Maternal among Deaths of Females of reproductive age (PMDF) for countries without reliable data (World Bank, WHO, UNFPA, UNICEF, 2010). For example, the MDG 5 indicators for maternal health are the MMRatio and proportion of births attended by skilled health personnel (UN Statistics Division, 2008). These measures do not consider the time, after pregnancy, that the maternal deaths are occurring. Also, deaths in a particular period do not usually match the risk of that period: These overlaps obviously have effect on these measures. Moreover, like most central rates, they are influenced by the population composition and therefore do not allow for fair comparisons among countries except when standardized. Additionally, these estimates do not take into account the number of women who were susceptible due to pregnancy but rather some proxy measure, based on some assumptions, making these measures questionable as a representative summary value that adequately describes the essential features required. For instance, MMRatio, which is the most widely used among these estimates, gives a false sense of precision. While this measure is intended to estimate obstetric risk, the measure is more a gauge of risk in

terms of “woman per child” rather than “woman per pregnancy” (World Bank, UNICEF, WHO, UNFPA, 2010). The denominator of this estimator is deceptive and should rather be the number of pregnant women during the period, which is impossible to determine and hence the use of total live births as its estimate (Nuamah, 2007). MMRate on the other hand, does not only reflect the risk of maternal deaths per pregnancy but also, per fertility. The denominator in this measure is exaggerated to include all women in the fertility age. While Lifetime Risk of maternal mortality, a measure of cumulative loss of human life due to maternal death over the female life course, is preferred to MMRatio and MMRate as a measure of the impact of maternal mortality, this measure can be defined and calculated in more than one way. Furthermore, its usual calculation without age specific data makes it not useful for comparability (WHO, 2009). In most developing countries, maternal mortality estimates are usually obtained by adjustment to deaths for women of reproductive age due to unavailable or unreliable data (Abouzahr, (1998); Hill, et al., (2007); World Bank, WHO, UNFPA & UNICEF, (2010)). Thus, the maternal mortality estimators in use are predictive, static, deterministic (without measurable variability), and do not adequately capture obstetric risks. There is therefore the need to develop better estimators (World Bank, UNICEF, WHO, UNFPA, 2010).

This study, focused on addressing the issue of good statistical estimators, is born out of the weaknesses of the estimators in use, and the apparent lack of research into the application of other methods. As stated in Luguterah & Nokoe, (2013), the challenge arising from having some censored data, at most one event occurring per subject and highly skewed observations, make the use of standard statistical techniques inappropriate: hence our proposal of the use of Survival analysis techniques. The application of Survival analysis techniques provides more informative estimates with measurable precision and is a much better way of estimating obstetric risk with broader Parametric and Non-parametric analytical prospects.

## **Methodology**

### **Survival Data Analysis**

In applying Survival analysis techniques to Maternal Mortality, we make the assumption that the time of maternal deaths are a function of a random process and therefore the time of death is a random variable with a probability distribution and consequently, other related distributions.

### Basic Concepts in Survival

Let  $T$ , denote the survival time of a woman from her time of conception. The distribution of  $T$  can be characterized by three equivalent functions (Lee & Wang, 2003).

*Survival Function,  $S(t)$*

$$\begin{aligned}
 & S(t) \\
 = & P(\text{a woman who has conceived surviving longer than time } t \text{ from conception}) \\
 & = P(T > t) \\
 S(t) = & 1 - P(\text{a woman who has conceived dying before time } t \text{ from conception}) \\
 & = 1 - F(t)
 \end{aligned}$$

$S(t)$  is a non increasing function of time with properties

$$S(t) = \begin{cases} 1 & \text{for } t = 0 \\ 0 & \text{for } t = \infty \end{cases}$$

*Probability Density function,  $f(t)$*

The probability density function of the survival time is defined as the limit of the probability that a woman dies in the short interval,  $t$  to  $t + \Delta t$ , per unit width,  $\Delta t$ , or simply the probability of dying in a small interval per unit time. It can be expressed as:

$$\begin{aligned}
 & f(t) \\
 = & \frac{\lim_{\Delta t \rightarrow 0} P[\text{a woman who has conceived dying in the interval } (t, t + \Delta t) \text{ after conception}]}{\Delta t} \\
 & = \frac{\lim_{\Delta t \rightarrow 0} P[x \in (t, t + \Delta t)]}{\Delta t}
 \end{aligned}$$

Where  $x$  denotes a woman who has conceived, dying

$f(t)$  is a non negative function such that;

$$f(t) = \begin{cases} \geq 0 & \text{for all } t \geq 0 \\ = 0 & \text{for all } t < 0 \end{cases}$$

*Hazard function,  $h(t)$*

The hazard function  $h(t)$ , which gives the conditional failure rate, is the probability of a woman who has conceived, dying in a small interval of time after conception assuming that the woman has survived to the beginning of that time interval.

$$\begin{aligned}
 h(t) = & \frac{\lim_{\Delta t \rightarrow 0} P \left[ \begin{array}{l} \text{a woman who has conceived dying in the interval } (t, t + \delta t) \\ \text{given that the woman has survived to } t \end{array} \right]}{\Delta t} \\
 & = \frac{\lim_{\Delta t \rightarrow 0} P[x_t \in (t, t + \Delta t)]}{\Delta t}
 \end{aligned}$$

Where  $x_t$  denotes a woman who has conceived, dying after she has survived to time  $t$

These functions are related by;

$$h(t) = \frac{f(t)}{S(t)}$$

### Estimating the Survival Functions

Survival functions can be estimated using a number of options; the Kaplan-Meier and the Life Table Method. In this study, the Life table

method, a non parametric method to estimate the survival functions was used. The method, which uses time intervals, estimates the survival functions up to the upper limit of each interval, and estimates the hazard and density functions at the midpoint of each interval (Gehan, 1969):

For the  $i^{th}$  interval, let  $t_i$  be the end time and  $q_i$  be the conditional probability of dying. Then;

$$\hat{S}(t_i) = \prod_{j=1}^{i-1} (1 - \hat{q}_j)$$

$$\hat{f}(t_{mi}) = \frac{\hat{S}(t_i) - \hat{S}(t_{i-1})}{b_i} = \frac{\hat{S}(t_i) \hat{q}_i}{b_i}$$

$$\hat{h}(t_{mi}) = \frac{d_i}{b_i(n_i - \frac{1}{2}d_i)} = \frac{2\hat{q}_i}{b_i(1 - \hat{p}_i)}$$

Where

$t_{mi}$  is the mid-point of the  $i^{th}$  interval,

$d_i$  is the number of women dying in the  $i^{th}$  interval after their conception,

$n_i$  is the number of women exposed in the  $i^{th}$  interval after conception,

$q_i = \frac{d_i}{n_i}$  is the conditional probability of a woman dying in the  $i^{th}$  interval after conception

$p_i = (1 - q_i)$  is the conditional probability of a woman dying in the  $i^{th}$  interval after conception

$b_i$  is the width of the  $i^{th}$  interval

The standard error of the survival function, Greenwood (1926) is estimated by:

$$s.e.(\hat{S}(t_i)) \approx \hat{S}(t_i) \sqrt{\sum_{j=1}^{i-1} \frac{\hat{q}_j}{n_j(1 - \hat{q}_j)}}$$

While that of the hazard function, Gehan (1969), is estimated by;

$$s.e.(\hat{h}(t_{mi})) \approx \hat{h}(t_{mi}) \sqrt{\frac{\left\{1 - \left[\frac{1}{2}\hat{h}(t_{mi})b_i\right]^2\right\}}{n_i\hat{q}_i}}$$

The probability density function, Gehan (1969), is estimated by;

$$s.e.(\hat{f}(t_{mi})) \approx \hat{S}(t_i)\hat{q}_i \sqrt{\frac{\left(\sum_{j=1}^{i-1} \frac{\hat{q}_j}{n_j(1 - \hat{q}_i)} + \frac{(1 - \hat{q}_i)}{n_i\hat{q}_i}\right)}{b_i}}$$

### Modeling and other Tests based on Survival Techniques

Once the survival functions have been developed, various tests and the modeling of Maternal Mortality, as well as the determination of the

appropriate distributions that best describes maternal Mortality can be done, using both the parametric and non parametric methods (See Lee & Wang, (2003)). These include the identification of prognostic factors through the log rank test, the assessment and modeling of the prognostic factors through regression analysis and the determination of an appropriate distribution for maternal survival.

**The Log-rank test**

The Log-rank test (Peto & Peto, 1972), a non parametric test of difference for survival functions, is the most widely used technique when data is censored. It measures the difference in the survival for the different groups at each of the given times. For a  $k$  factor group, this test the hypothesis that;

$$H_0: S_1(t) = S_2(t) = \dots = S_k(t) \quad \text{for all } t$$

$$H_1: \text{ not all } S_j(t) \text{ are equal.} \quad j = 1, 2, \dots k.$$

Where  $S_j(t)$  is the survival function for the  $j^{th}$  group

This is tested as a chi-square test which compares the observed numbers of failures to the expected number of failure under the hypothesis. Thus, given that  $O_j$  and  $E_j$  is the observed and expected number of deaths respectively for the  $j^{th}$  group, the test statistic is given by;

$$\chi^2 = \sum_{j=1}^k \frac{(O_j - E_j)^2}{E_j}$$

where

$$E_j = \sum_{\substack{\text{all } t \\ n_{jt}}} e_{jt}$$

$$e_{jt} = \frac{n_{jt}}{\sum_{\text{all } j} n_{jt}} \times d_t$$

$n_{jt}$  is the number of women still exposed to the risk of dying at time up to  $t$  for the  $j^{th}$  group

$d_t$  is the total number of deaths for all groups at time  $t$ . Thus

$$d_t = \sum_{\text{all } j} d_{jt}$$

has approximately a chi-square distribution with  $k - 1$  degrees of freedom. A large chi-square value will lead to a rejection of the null hypothesis in favor of the alternative that the  $k$  groups do not have the same survival distribution.

*Proportional Hazard Regression*

The Cox proportional regression (Cox, 1972) was used to determine the effect of some socio economic and demographic factors on maternal

survival based on the assumption of proportionality. In this model, the hazard for an individual is assumed to be related to the covariates through the equation;

$$h_i(t) = \lambda_0(t)\exp\{\beta_1x_{i1} + \dots + \beta_kx_{ik}\}$$

Taking the logarithm of both sides, the model can also be written as

$$\log h_i(t) = \alpha(t) + \beta_1x_{i1} + \dots + \beta_kx_{ik}$$

Where  $\alpha(t) = \log \lambda_0(t)$ .

The ratio of the hazard for two individuals  $i$  and  $j$  (say rural women and urban women) is then given by;

$$\begin{aligned} \frac{h_i(t)}{h_j(t)} &= \frac{\lambda_0(t)\exp\{\beta_1x_{i1} + \dots + \beta_kx_{ik}\}}{\lambda_0(t)\exp\{\beta_1x_{j1} + \dots + \beta_kx_{jk}\}} \\ &= \exp\{\beta_1(x_{i1} - x_{j1}) + \dots + \beta_k(x_{ik} - x_{jk})\} \end{aligned}$$

Where  $\beta_1, \dots, \beta_k$  measures the relative risk for the  $i^{th}$  woman over the  $j^{th}$ , with respect to the change in the  $x_l^{th}$  covariate,  $l = 1, \dots, k$  respectively.

### Determination of an appropriate distribution

Graphical and analytical methods exist for the determination of an appropriate distribution for survival data. In this study, the hazard plotting technique (Nelson, 1972), a graphical plotting technique designed to handle censored data was used.

The shape of a hazard plot gives a good indication of the distribution that could best fit it: For instance, a constant hazard would suggest an exponential distribution; while a first increasing and then decreasing hazard would suggest a log normal or log-logistic model, a monotonically decreasing function would suggest a log-logistic model; The Weibull distribution could have an increasing, decreasing or constant hazard. The monotonically increasing shape of the hazard plot for maternal mortality, suggests the assumption that maternal survival had a Weibull distribution.

The parameters of the assumed Weibull distribution were then estimated using the hazard plotting technique. The adequacy of the fit was also assessed using the R-squared value of the linear plot of  $\log(t)$  against  $\log H(t)$ :  $H(t)$  is the cumulative hazard at time  $t$ .

### Data Collection

The data for this study was obtained from the Ghana statistical Service and was collected in the Ghana Maternal health survey 2007. The Survey was jointly implemented by the Ghana Statistical Service and the Ghana Health Service with technical assistance from the Macro International, a U.S.A based company. The Survey which was the first of its kind in Ghana is considered as the first nationally representative survey to collect comprehensive information on maternal morbidity and mortality in

the country. A two phase approach of collecting the required information from enumeration areas (clusters) was used with a sample of 240,000 households, randomly sampled across Ghana, to obtain information on all maternal deaths in the households in phase one: A total of 4,203 women aged 12 to 49 were identified as dead in these households. In phase two, a verbal autopsy of all deaths identified in phase one was conducted using the sisterhood method as well as information from a sub sample of 10,370 women aged 15-49 years, on a wide range of maternal health issues pertaining to pregnancies, live births, abortions and miscarriages, etc.

Survival analysis typically follows a group of people from beginning to the end of a study to observe when each member of the group will fail: This cohort is known as a stationary cohort. However, in this study, observations over a single cross section of time is used and manipulated to represent a cohort. In this cross sectional cohort, different individuals may have different start points within the selected study time frame; however, the estimates derived provide estimates of current trends in survival: the time frame used in this study is 2002 to 2007.

In order to estimate maternal survival, a combination of the data for the verbal autopsy and the 10,370 women interviewed was used. Since the second phase was a sub sample of the first phase, only deaths that matched the households sampled in the second phase, by cluster, were considered. Of these, only conceptions within the 2002 to 2007 period and the maternal deaths resulting from these conceptions were used. The period from conception to the death of a woman was taken as the uncensored data while the censored data was the period from conception to the date the data was collected or up to one month after delivery (whichever came first). All the data were collected in months and all censored data are right censored. These derived time variables were used to estimate the survivorship, fit distributions and perform other tests.

## **Results and Discussion**

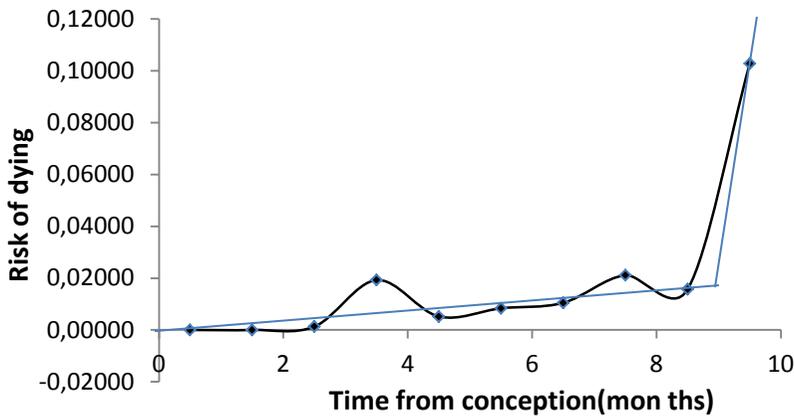
Table 1 summarizes the survival estimates with their measures of precision. It shows that, in Ghana, approximately 92 percent of pregnant women make it through to delivery while 83 percent make it to the end of the postpartum period: This means a maternal mortality of 17 percent. Approximately 9 percent of women, who conceived, lost their lives during the first month after delivery: representing over 50 percent of the total maternal deaths. This makes the first month after delivery the most risky period for a pregnant woman. Thus a Ghanaian woman, once pregnant, has approximately a 1 in 10 chance of dying before delivery, and a 2 in 10 chance of dying by the end of the ten month after conception (up to one month after delivery). Accordingly, if a pregnant Ghanaian woman delivered

safely, she still had approximately a 1 in 10 chance of dying within one month after delivery. A focus therefore on a mother’s health immediately after she was delivered and up to one month thereafter, could reduce maternal mortality by up to half.

As shown by the hazard plot (Fig 1) maternal mortality increased at an increasing rate. This plot also suggests a possible two part mortality trend: the period before delivery and the period after delivery, with the later being more perilous. The results of the Log-rank tests shown in Table 2 show that, Type of town, ever given birth and the marital status of a woman, are all associated with maternal mortality. The results of the Cox regression (Table 3) show that a mother who has ever given birth has a 67 percent less risk of dying due to pregnancy related issues than a woman who has never given birth. Generally, as a woman grows older, the risk of dying decreases by 4.5 percent for every additional year of age: These results are statistically significant. Area differences were also significant with rural folks having a 67 percent less risk than town folks, while small and large cities had 31.4 and 44.7 percent more risk respectively, than town folks: Thus the more urban the locality, the higher the risk of maternal deaths. This could be a reflection of interventions in rural communities to make motherhood safer or of data inadequacies or unreliability. The estimated parameters of the fitted Weibull distribution, and its appropriateness, are also shown in Table 4. The results show that, the Weibull distribution describes maternal Survival very well.

Table 1. Maternal Survival Estimates

Time from conception (month)	Probability of failure	S.E.	Survival probability	S.E.	Hazard	S.E.	Density	S.E.
0 to 1	0.00000	0.00000	1.00000	0.00000	0.00000	*	0.00000	*
1 to 2	0.00000	0.00000	1.00000	0.00000	0.00000	*	0.00000	*
2 to 3	0.00131	131	0.99869	131	131	131	131	131
3 to 4	0.01908	524	0.97964	539	926	534	905	523
4 to 5	0.00519	299	0.97456	611	520	300	508	293
5 to 6	0.00833	415	0.96643	728	837	418	812	404
6 to 7	0.01042	518	0.95637	878	047	524	007	501
7 to 8	0.02091	845	0.93637	179	113	862	999	808
8 to 9	0.01554	890	0.92182	429	567	904	456	834
9 to 10	0.09778	800	0.83168	886	280	096	013	585



**Fig 1. Hazard plot for Maternal Survival against time**

**Table 2: Log-Rank Test of Differences in Maternal survival**

	Variable	$\chi^2$ Value	D. F	P-Value
1	Ever Given Birth	4.57635	1	0.032
2	R3M Region	0.26477	1	0.607
3	Urban/ Rural	1.27181	1	0.259
4	Mother Ever schooled	0.10888	1	0.741
5	Marital Status	6.11932	3	0.047
6	Type of Town	19.12600	3	0.000
7	Age of Mother at birth	6.26820	4	0.180
8	Mother's total number of Births	111.64800	8	0.000
9	Region	6.17270	9	0.723

**Table 3. Maternal Cox Regression**

	$\beta$	S.E.	Wald	DF	Sig.	Exp( $\beta$ )
Town (Compared to Large City)	0.369	0.363	1.036	1	0.309	1.447
Rural	-0.950	0.271	12.242	1	0.000	0.387
Small City	0.273	0.454	0.361	1	0.548	1.314
Ever attended School(Compared to never)	0.214	0.264	0.661	1	0.416	1.239
Ever given birth(Compared to never)	-0.843	0.254	11.041	1	0.001	0.430
Age of mother at Pregnancy	-0.046	0.017	7.478	1	0.006	0.955

**Table 4. Summary of fitted distribution for Maternal Survival**

Variable	Assumed Distribution	Parameter Estimates	R <sup>2</sup> Estimate
Maternal Survival	Weibull	$\gamma = 1.79019,$ $\lambda = 0.02657$	0.9714

**Limitations**

As in most maternal mortality studies in developing countries, data inadequacies and reliability are the main limitations to this study. For

instance, the zero recorded for maternal deaths in the first two months after conception are most likely a reflection of the lack of information than an indication of absolutely no maternal risk. These inadequacies and unreliability will not affect the methodology proposed in this study but could have an effect on the precision of the estimates in this study, and definitely affected the ability to test for the influence of other important prognostic factors.

## Conclusion

Several methods exist for the assessment of maternal mortality but most of these methods usually use central rates. These static measures do not adequately capture, what they are intended to represent. This study has demonstrated that survival techniques, which are dynamic measures, can be applied to the study of maternal survival. This technique does not only provide adequate representation and more information than the maternal mortality rates, which are widely used, but also give precision for their estimates and enable the modeling of maternal mortality; consequently, a model was developed for maternal survival.

It was shown in this study that, maternal survival and hence mortality, is adequately described by a Weibull model. The Weibull distribution which described maternal survival, had shape and scale parameters,  $\gamma, \lambda, > 0$ , indicating an increasing risk of mortality with time and thus a hazard that increases at an increasing rate: The prognostic factors that influence the hazard, and hence survival, are the determinants of the parameters of this model. In this study, the shape and scale parameters for the Weibull distribution that described maternal survival for this data was determined to be  $\gamma = 1.79019$  and  $\lambda = 0.02657$  respectively.

The application of Survival Analysis Techniques to the study of maternal mortality allows for a wide range of statistical tests and modeling, both from the parametric and Non-parametric fronts.

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