INTRODUCTION
Graves’ disease is an autoimmune disorder that causes hyperthyroidism, or overactive thyroid (NIDDK 2017). With this disease, the immune system attacks the thyroid and causes it to make more thyroid hormone than the body needs. Thyroid hormones regulate the body’s energy utilization, which has an impact on all bodily organs and even the heartbeat. Hyperthyroidism can lead to severe issues with the heart, bones, muscles, menstrual cycle, and fertility if treatment is not received. Untreated hyperthyroidism during pregnancy can cause health issues for both the mother and the unborn child. Graves’ disease can also affect eyes and skin NIDDK (2017). Thus, this research focused on Graves’ disease (toxic Goiter) and some variable that contribute towards the increase of the disease in Nigeria. It is reported that 3% of female and 0.05% of male were experiencing Graves in their lifetime (Adelleye et al., 2020). Weight loss despite an increase in appetite, heat sensitivity, irritability, sleeplessness, sweating, hyperreflexia, palpitations, muscle weakness, and irregular menstruation are among the basic signs of hyperthyroidism. Diffuse goiter, fine resting tremor, tachycardia, hyperreflexia, lid lag, warm, smooth skin, and proximal myopathy are examples of clinical symptoms. Depending on the situation, antithyroid medications, radioablative therapy, or thyroidectomy are among the treatment options typically provided to individuals with Graves’ disease (Adelleye et al., 2020). According to current studies, there are one or two cases of Graves’ illness for every 1,000 people in England each year. Compared to the previously reported rate of roughly 0.3 occurrences per 1,000, this rate is significantly higher. Compared to men, women experience it far more frequently (Feingold et al., 2015). Classical signs of hyperthyroidism include weight loss of greater than 6%, which is about equal to the combined effects of idiopathic hyperthyroidism, Hashimoto’s thyroiditis, and Graves’ disease. (Feingold et al. 2015) It was discovered that 2.7% of women and 23% of males had either a history or a present case of Graves’ illness. Additionally, 15% of women reported having goiter, 10.3% had antithyroid antibodies, and around two-thirds of women had hyperthyroidism compared to Graves’ illness. According to a recent report in this area, the annual incidence of 80 cases per 100,000 women is still present. According to the “HANES” study, the prevalence of hyperthyroidism is 0.7% at the sub-clinical level and 0.5% at the clinical level. Information confirms that there is a > 6% lifetime incidence of autoimmune thyroid disease, which is about equal to the sum of Hashimoto's thyroiditis, idiopathic hyperthyroidism, and Graves’ disease (Feingold, et.al. 2015). An growth of the thyroid gland is called a goiter. That is the gland located right below the Adam’s apple at the front of the neck. It can just be a passing issue that goes away on its own, or it might be a sign of another thyroid illness that could be more serious and need medical attention. Since many things can make a thyroid swell, there are lots of types of Goiters. A few of them are: Simple Goiters, Endemic Goiters, Sporadic or nontoxic Goiters and Multinodular Goiters.

A Goiter is described as ”toxic” when it’s linked to hyperthyroidism. That means the thyroid makes too much thyroid hormone. A “nontoxic” Goiter does not cause either hyperthyroidism or hypothyroidism (Nazario, 2021). Elvan et al, (2010) compared five models (Gampertz, Gamma Log-logistics, Weibull and Log-normal) using breast cancer data. The result of the study showed that Gampertz model was the most suitable model to fit their data. Anet and Nestor (2011) carried out research on the application of hazard model for patient with breast cancer in Cuba using 6381 patients to compare six models (Gampertz, Exponential, Weibull, Log-logistics, Log-normal and Generalize Gamma). Their result showed that Gampertz model fit data well. Log-logistics distribution is an important survival parametric model that is used in the field of science, actuarial hydrology, survival analysis, reliability and the Economics (Al shorani, et al 2016). According to Bennett, (1983) although the structure of the log-logistics distribution and the log-normal distribution are extremely similar, the log-logistic distribution is more suited for survival analysis when data contains censored observations than the log-normal distribution. The lognormal model gives a fully stated probability distribution for the observations as well as a reasonable estimate of the variance explained by the model, a number that the Cox model is debatable about. The Cox and lognormal models’ results are compared, and they appear to differ to some extent, it is concluded that, if the lognormal model correctly fits the data, it may be a useful method for analyzing censored
survival data. (Royston, 2001). Hui (2011) evaluated Weibull and Cox models in a study of stomach cancer patients and found that the Weibull model suited the data better than the Cox model.

All these above-mentioned authors have a difference in either using the models or the data in the diseases they used for the analysis compared to the present study. Thus, the study focused on semi-parametric, and parametric models for analysis and data used for research on Graves’ disease (toxic).

Toxic thyroid carcinoma should be suspected especially in male patients older than 50 years presenting with a typical, recurrent, highly symptomatic thyrotoxicosis. Patients with ToxTc seemed clinical resistant, therefore requiring higher amount of therapeutic radioactive and presenting a higher clinical morbidity (Als et al 2002).

The two methods that contributed significantly to the development of the survival analysis. The first is Kaplan and Meier who introduced an estimator for survival probabilities. Second is Cox who introduced what is now called the Cox Proportional Hazard Model (CPHM), which is a regression model. Both models are heavily used to date and belong to the toolbox of every data scientist. Initially presented by Boag (1949) and Berkson & Gage (1952), the mixture cure model is a usually used tool for assessing both the proportion hazard model is used in \( S(t/x) \) estimation, the model described as the accelerated failure mixed cure model.

(Bog 1949) Studied the case when \( S(t/x) \) is modeled as log normal., (Farewell, 1982) studied the latency part \( S(t/x) \) is modeled by Weibull distribution., (Denham et al, 1996) studied another case with log normal assumed \( S(t/x) \). The mixture cure model by assuming a proportion hazard model for \( S(t/x) \) with unspecified baseline hazard function (Peng & Dear, 2000) and (Sy & Taylor, 2000).

The advantage of the mixed cure model is that it enables the separation modelling of the cure distribution of both the cured and uncured individuals. Generally, using the logit function, the effect of \( z \) covariant is modelled with

\[
\pi(z) = \frac{\exp(bz)}{1+\exp(bz)}
\]

The b in the formula is the vector of unknown parameters. The effects of \( z \) covariates modelled with log(-log(1-\( \pi(z) \))) = bz by using log-log. When probity function is used, it is modelled as \( (\pi(z)) = bz \). The term \( \Phi() \) is the cumulative probability function of the standard normal distribution.

In computational method, Let \( O = (y_i, \delta_i, z_i, x_i) \) denote the observed data for the \( i \)th individual \( i = 1, \ldots , n \), where \( z_i, x_i \) are the possible covariates in the incidence and latency parts respectively. We consider the censorship to be impartial land non educational. It is important to note that even though we use distinct covariate notations for the incidence and delay components, the same let \( \Theta = (b, \beta, S_p(i)) \) denote the unknown parameters. To use the EM algorithm to estimate unknown parameters in this PH mixture cure model, let \( y_i \) be an indicator of cure status of the \( i \)th patient, namely, \( y_i = 1 \) if the patient is uncured and 0 otherwise, \( i = 1, 2, \ldots , n \). Obviously, if \( \delta_i = 1, y_i = 1 \); if \( \delta_i = 0, y_i \) is not observable and it can be one or zero. Note that \( \pi(z) = P(y_i = 1/z) \).

Let \( y = (y_1, y_2, \ldots , y_n) \) Therefore, \( y \) is partially missing information which will be employed in the EM algorithm. Given \( y = (y_1, y_2, \ldots , y_n) \) and \( O \), the complete likelihood function can be expressed as;

\[
\Pi_{i=1}^{n}[1-\pi(z_i)]^1-y_i \pi(z_i)^y_i \theta(t_i|Y = 1, x_i) S(t_i|Y = 1, x_i)
\]

(3)

Where \( h(·) \) is the hazard function corresponding to \( S(·) \). The logarithm of the complete Likelihood function can be written as \( l(c(b(\beta, \Theta, O), y) = l c(1(b(\beta, O), y) + l c(2(b, O, y) \),

Where, \( l c(1(b(\Theta, O, y) = \sum_{i=1}^{n} y_i \log[\pi(z_i)] + (1- y_i) \log [1- \pi(z_i)] \)

\[
l c(2(b, \beta, O, y) = \sum_{i=1}^{n} \delta_i \log[h(t_i|Y = 1, x_i)] + y_i \log [S(t_i|Y = 1, x_i)]
\]

(5)

Given the observed data \( O \) and current estimations of parameters \( \Theta = (b_0, b_1|Y = 1, x_i) \), the E-step in the EM method computes the conditional expectation of the entire log-likelihood with regard to \( y_i \)'s. This phase can be finished using the conditional expectation of \( y_i \) because (1.4) and (1.5) are both linear functions of \( y_i \). The following describes the predicted value of \( E(y_i|O, \Theta^{(m)}) \).

\[
w_i^{(m)} = E(y_i|O, \Theta^{(m)}) = \delta_i + (1- \delta_i) \frac{\pi(z_i|S_i(t_i|Y = 1, x_i))}{1-\pi(z_i|S_i(t_i|Y = 1, x_i))} S(t_i|Y = 1, x_i)
\]

(6)

It is easy to see that \( w_i^{(m)} = 1 \) if \( \delta_i = 1 \) and \( w_i^{(m)} \) is the probability of uncured patients if \( \delta_i = 0 \). Thus, the another part of \( E(y_i|O, \Theta^{(m)}) \) can be interpreted as the conditional probability of the \( i \)th individual remaining uncured. Because
\( \delta_t \log w_r^{(m)} = 0 \) and \( w_r^{(m)} = \delta_t \), the expectations of (1.4) and (1.5) can be written as

\[
E(I_{CL}) = \sum_{i=1}^{n} \delta_i \log [\pi(x_i)] + (1 - w_i^{(m)}) \log [1 - \pi(x_i)]
\]

(7)

\[
E(I_{CL}) = \sum_{i=1}^{n} \delta_i \log [w_i^{(m)} h(t_i)] + w_i^{(m)} \log [S(t_i)]
\]

(8)

The Weibull Distribution

The Weibull model (invented by Waloddi Weibull in 1939) is a common descriptive two-dimensional model. The model’s second parameter gives it more flexibility and a different risk function. The Weibull model’s usefulness for performance work is determined in part by its flexibility, and in part by the ease with which risk and survival functions may be calculated. Weibull Distribution is useful in a wide range of situations. The most useful methods which are considered to be the traditional methods are maximum likelihood and the moment estimation (Cohen and Whitten, 1982).

Survivals function

\( s(t) = \exp(-\lambda t)^p \) Lawless(2011)

Where \( \lambda = \exp(x, \beta) \)

(9)

\[
s(t) = \exp(-\lambda t)^p\]

(10)

The hazard function is \( f(t) = \lambda p(\lambda t)^{p-1} \exp(-\lambda t)^p \)

(12)

The expected duration from Weibull is

\[ E(T) = \left( \frac{1}{\lambda} \right)^{\frac{1}{p}} \Gamma \left( 1+\frac{1}{p} \right) \]

(13)

Where \( \Gamma \) denotes gamma function.

Where \( p \) and \( \lambda \) are the scale and shape parameters respectively.

Log-normal Distribution

Continuous probability distribution of a random variable whose logarithm is normally distributed is known as a log-normal distribution in probability theory. By the definition of Lognormal, if \( \sigma \ln(X) \) has normal distribution \( X \) has Log-normal distribution. That is, if \( X \) is normally distributed exp \( X \) (log normally distributed. If \( Y \) is normally distributed with mean 0 and variance \( \sigma \), then the random variable \( X \) defined by the relationship \( Y = \log(X) \) is distributed as Log-normal, and is denoted as lognormal (0, \( \sigma^2 \))

\[ Y = \ln(X) \] has a normal distribution if the random variable \( X \) is log-normal distributed (Eric W 2020).

\[
S(t) = 1 - \rho(\lambda t) ^ p \]

\[
h(t) = \frac{\lambda \exp(-\lambda t)^p}{\sqrt{2\pi\sigma^2}} \exp\left(-\frac{\ln^2(\lambda t)}{2\sigma^2}\right) \]

(14)

\[ f(t) = \frac{\lambda \exp(-\lambda t)^p}{\sqrt{2\pi\sigma^2}} \exp\left(-\frac{\ln^2(\lambda t)}{2\sigma^2}\right) \]

(15)

The expected life time and its are given by:

\[ E(T) = \exp(\mu+\frac{\sigma^2}{2}) \]

(17)

where \( \mu \) and \( \rho \) denote this distribution’s scale and shape respectively.

RESULTS AND DISCUSSION

Comparison of the Cox mixed cure model with the Weibull and Lognormal

The result obtained from semi parametric model (Cox mixed cure model) and parametric models (weibull and lognormal) are compared using Akaike information criterion (AIC). The results for the models are shown below.

<table>
<thead>
<tr>
<th>Covariate-</th>
<th>HR</th>
<th>Standard Error</th>
<th>P-Value</th>
<th>95% C.I. Min</th>
<th>95% C.I. Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>0.7394</td>
<td>0.4662</td>
<td>0.0410</td>
<td>0.2211</td>
<td>1.2200</td>
</tr>
<tr>
<td>Age at diag</td>
<td>0.5237</td>
<td>0.0204</td>
<td>0.0148</td>
<td>-1.380</td>
<td>0.1666</td>
</tr>
<tr>
<td>T3</td>
<td>0.6275</td>
<td>0.4660</td>
<td>0.3810</td>
<td>0.2211</td>
<td>1.2200</td>
</tr>
<tr>
<td>T4</td>
<td>0.6679</td>
<td>0.0059</td>
<td>0.0164</td>
<td>0.3700</td>
<td>0.7125</td>
</tr>
<tr>
<td>TSH</td>
<td>0.4833</td>
<td>-0.0446</td>
<td>0.3333</td>
<td>-1.3400</td>
<td>0.1796</td>
</tr>
</tbody>
</table>

Log likelihood = -209.30311, Scale= 0.581
Log lik(model)= -63  Log lik(intercept only)= -65.9
Chisq= 5.75 on 5 degrees of freedom, p= 0.33

<table>
<thead>
<tr>
<th>Covariate-</th>
<th>HR</th>
<th>Standard Error</th>
<th>P-Value</th>
<th>95% C.I. Min</th>
<th>95% C.I. Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Diag</td>
<td>0.0146</td>
<td>0.0122</td>
<td>0.0155</td>
<td>0.433</td>
<td>0.780</td>
</tr>
<tr>
<td>Sex</td>
<td>0.2983</td>
<td>0.4059</td>
<td>0.3818</td>
<td>0.288</td>
<td>1.060</td>
</tr>
<tr>
<td>T3</td>
<td>0.0528</td>
<td>0.0456</td>
<td>0.0462</td>
<td>0.324</td>
<td>0.990</td>
</tr>
<tr>
<td>T4</td>
<td>0.0359</td>
<td>0.0271</td>
<td>0.0192</td>
<td>0.155</td>
<td>1.42</td>
</tr>
<tr>
<td>TSH</td>
<td>0.0027</td>
<td>0.0207</td>
<td>0.0358</td>
<td>0.564</td>
<td>0.580</td>
</tr>
</tbody>
</table>

(Intercept) 1.5764, 0.7277, 2.17 0.030
Log(scale) -0.3509, 0.1429 -2.46 0.014, Scale=0.704

<table>
<thead>
<tr>
<th>Covariate-</th>
<th>HR</th>
<th>Standard Error</th>
<th>P-Values</th>
<th>95% C.I. Min</th>
<th>95% C.I. Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Diag</td>
<td>0.0330</td>
<td>1.0336</td>
<td>0.0258</td>
<td>0.1970</td>
<td>1.2900</td>
</tr>
<tr>
<td>Sex</td>
<td>0.8523</td>
<td>0.4264</td>
<td>0.6462</td>
<td>0.1870</td>
<td>1.3190</td>
</tr>
<tr>
<td>T3</td>
<td>0.0559</td>
<td>0.9455</td>
<td>0.0783</td>
<td>0.7140</td>
<td>0.4750</td>
</tr>
<tr>
<td>T4</td>
<td>0.9750</td>
<td>0.0252</td>
<td>0.0293</td>
<td>-0.859</td>
<td>0.3900</td>
</tr>
<tr>
<td>TSH</td>
<td>1.0695</td>
<td>0.0672</td>
<td>0.0581</td>
<td>1.1560</td>
<td>1.1560</td>
</tr>
</tbody>
</table>

Likelihood = 6.21
df, p=0.28
Our investigation in table 1, (Weibull model) revealed that sex, age at diagnosis and thyroxine (T4) showed it is statistically significant which related to the finding of Bijan et al. (2008). Except Triiodothyronine (T3) showed it is insignificant. Also found that sex is insignificant in Cox mixed model and Log-normal models.

CONCLUSION
Based on the investigation of Comparative Analysis of the Cox Mixed Cure model with Parametric Models, it concluded that Cox mixed cure model is the suitable model for estimating survival of toxic goiter. It is also the efficient model to be used to minimize toxic goiter using semi parametric and parametric models. Cox-mixed cure models should be used to carryout Grave’s Disease survival analysis, due to the fact that it gives the best fit for survival analysis

REFERENCES
COMPARATIVE ANALYSIS OF ...

Usman et al.,


