

PARAMETRIC SURVIVAL MODELS WITH INTERVAL CENSORED DATA IN
DETERMINING PROGNOSTIC FACTORS OF PATIENTS OF LUNG CANCER

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Dedicated to my beloved father and mother,
Muhamad Jamil Bin Rosdi and Kalsom Binti Husin for their endless moral, financial support from the beginning until the end of my study.

To my siblings,
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ABSTRACT

In clinical trials, biological research and medical studies that involved periodically follow-ups, it is predominantly to have censored data. The censored data can be either left, right or interval censored where it reflects on the uncertainty of survival time until an event occur. Survival analysis can accommodates both fixed and time varying covariates with the presence of censored data. The survival time of parametric distribution of Weibull, exponential and log-logistic were derived by using the inverse cumulative distribution function with the hazard and survival function. Standard estimation values such as, the mean square error (MSE), root mean square error (RMSE), mean absolute error (MAE), and mean absolute percentage error (MAPE) were employed in comparing different distributions and number of sample sizes. Besides, Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), Corrected Akaike Information Criterion (AIC_C) been evaluated in finding the best fit model towards the survival time of lung cancer. Thus, the exponential model was found to be the most reliable with censored and fixed covariate of simulation and lung cancer data while the log-logistic appeared to be practically more stable than Weibull in estimating the censored with varying effect covariate. Meanwhile, the prognostic factors that were significant involved the types of lung cancer, gender and some other interactions. Somehow, increased number of sample either in simulation or bootstrap makes the results to be approximately more reliable as the biases decreased.



ABSTRAK

Dalam ujian klinikal, penyelidikan biologi and kajian perubatan yang melibatkan tindakan lanjut secara berkala, ia mempunyai peluang yang lebih besar untuk mendapat data yang disensor. Sensor data sama ada kiri, kanan atau selang ditapis dimana ia mencerminkan ketidakpastian masa hidup sehingga berlaku kejadian. Analisis survival boleh menampung kovariat tetap dan masa yang berbeza dengan kehadiran data yang sensor atau data yang ditapis. Masa kelangsungan parametrik Weibull, exponential and log-logistik diperoleh dengan menggunakan kaedah fungsi pengedaran kumulatif songsang dengan fungsi bahaya dan kelangsungan hidup. Nilai-nilai seperti min kesilapan (MSE), min akar kesilapan (RMSE), kesilapan ralat mutlak (MAE), kesilapan peratusan absolute (MAPE) digunakan untuk membandingkan sensor data dengan bilangan saiz sampel yang berbeza. Selain itu, Kriteria Maklumat Akaike (AIC), Kriteria Maklumat Bayesian (BIC), Kriteria Maklumat Akaike (AICC) yang diperbetulkan telah diperiksa untuk mencari model yang sesuai untuk kanser paru-paru. Oleh itu, model eksponen didapati paling dipercayai dengan kovariat yang disensor, dan tetap bagi data simulasi dan data kanser paru-paru manakala log logistik kelihatan lebih stabil daripada Weibull dalam menganggarkan yang disensor dengan pelbagai kesan kovariat. Sementara itu, faktor prognostik yang penting melibatkan jenis paru-paru, jantina dan beberapa interaksi lain antara kovariat. Tambahan lagi, peningkatan saiz sampel dalam simulasi dan bootstrap menjadikan keputusan analisis lebih baik apabila bias atau anggaran kesilapan kesilapan semakin menurun.



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LIST OF SYMBOLS

α	- Alpha (Maximum rate)
β	- Beta (minimum rate)
θ	- Theta
a	- Shape parameter
e	- Estimation error ($Y_i - \hat{Y}_i$)
b	- Scale parameter
λ	- Lambda
n	- Number of sample
N	- Number of population
NaN	- Not a number
Inf	- Infinity
ρ	- Correlation coefficient
ϕ	- Degrees of freedom
ℓ	- Log-likelihood function
δ	- Delta
Σ	- Sum
L_i	- Left censored
R_i	- Right censored
I_i	- Interval censored
δ_i	- Binary form for left and right censored
ρ_i	- Binary form for interval censored
t_i	- Time of survival
T_i	- Survival time
\propto	- Proportional to
DL_s	- Detection limits
$h(t)$	- Hazard function



- $s(t)$ - Survival function
 $H(t)$ - Cumulative hazard ($\Lambda(t)$)
 $F(t)$ - Probability density function
 $L(a, b)$ - Likelihood function
 HbA^{1c} - Glycated haemoglobin



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LIST OF ABBREVIATIONS

<i>AEL</i>	- Adjusted empirical likelihood
<i>AFT</i>	- Akaike Failure Time
<i>AIC</i>	- Akaike Information Criterion
<i>AIC_C</i>	- Corrected Akaike Information Criterion
<i>AIDS</i>	- Acquired Immune Deficiency Syndrome
<i>ASR</i>	- Age Standardised Incidence Rates
<i>BIC</i>	- Bayesian Information Criterion
<i>BMI</i>	- Body Mass Index
<i>CCC</i>	- Concordance correlation coefficient
<i>CCRT</i>	- Chemoradiotherapy
<i>CMV</i>	- Cytomegalovirus infection
<i>CMLE</i>	- Consistent maximum likelihood estimator
<i>DGP</i>	- Data generating process
<i>EM</i>	- Expectation maximisation algorithm
<i>ESLD</i>	- End-stage liver disease
<i>EL</i>	- Empirical likelihood
<i>FC</i>	- Fixed covariate
<i>GLM</i>	- Generalised Linear Model
<i>HIV</i>	- Human immunodeficiency virus
<i>HDI</i>	- Human development index
<i>ICER</i>	- In-cost effectiveness ratio
<i>IARC</i>	- International Agency for Research on Cancer
<i>KM</i>	- Kaplan-Meier
<i>LC</i>	- Lung cancer
<i>LOD</i>	- Limit of detection
<i>LRT</i>	- Likelihood ratio test
<i>MAKNA</i>	- National cancer society in Malaysia

<i>MLE</i>	- Maximum Likelihood Estimation
<i>MAE</i>	- Mean absolute error
<i>MAPE</i>	- Mean absolute percentage error
<i>MBE</i>	- Mean bias error
<i>MSE</i>	- Mean square error
<i>MSMLE</i>	- Modified semiparametric maximum likelihood estimator
<i>MICE</i>	- Multiple imputation chained equation
<i>MIDMLE</i>	- Midpoint maximum likelihood estimator
<i>MSV</i>	- Model selection variance
<i>NA</i>	- Nelson-aelan
<i>NCR</i>	- National cancer registry
<i>NRIM</i>	- Newton Raphson iterative method
<i>NSCLC</i>	- Non-small cell lung cancer
<i>NPMLE</i>	- Non-parametric maximum likelihood estimator
<i>NBFH</i>	- Non-parametric Behrens- Fisher hypothesis
<i>ODS</i>	- Outcome dependent sampling
<i>PH</i>	- Proportional hazard
<i>PIC</i>	- Partly-interval censored data
<i>PAH</i>	- Polycyclic aromatic hydrocarbon
<i>PO</i>	- Proportional odds
<i>QOL</i>	- Quality of life
<i>RMSE</i>	- Root mean square error
<i>RNA</i>	- Ribonucleic acid
<i>RM</i>	- Reconstruction method
<i>SA</i>	- Sensitivity analysis
<i>ST</i>	- Score test
<i>SD</i>	- State dependent
<i>SCLC</i>	- Small cell lung cancer
<i>SE</i>	- Standard error
<i>TVC</i>	- Time varying covariate
<i>WLR</i>	- Weighted log rank
<i>WKM</i>	- Weighted Kaplan-Meier
<i>VTSABD</i>	- Virginia Twin Study of Adolescent Behaviour
<i>XRF</i>	- X-ray fluorescence



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12. Analysis of Parametric Survival Models in right censored data using simulation procedure.
13. Estimating Pteridophyta species diversity of abundance and occupancy by modelling zero-inflated count data.
14. Parametric Weibull Time-Varying Covariate Model for HIV-TB Mortality.

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