Weibull AFT Regression Functions in R

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Weibull accelerated failure time regression can be performed in R using the `survreg` function. The results are not, however, presented in a form in which the Weibull distribution is usually given. Accelerated failure time models are usually given by

$$\log T = Y = \mu + \boldsymbol{\alpha}^T \mathbf{z} + \sigma W,$$

where $\mathbf{z}$ are set of covariates, and W has the extreme value distribution. Given transformations

$$\begin{aligned} \gamma &= 1/\sigma, \\ \lambda &= \exp(-\mu/\sigma), \\ \boldsymbol{\beta} &= -\boldsymbol{\alpha}/\sigma, \end{aligned}$$

we have a Weibull model with baseline hazard of

$$h(x|\mathbf{z}) = (\gamma \lambda t^{\gamma-1}) \exp(\boldsymbol{\beta}^T \mathbf{z}).$$

Further, the `survreg` function generally gives $\log \sigma$, rather than σ as output. The function `WeibullReg` (along with `ConvertWeibull`) solves this problem. Hazard ratios ($\exp(\boldsymbol{\beta}_i)$) are additionally produced.

The function also produces the "event time ratio" (ETR, $\exp(-\boldsymbol{\beta}_i/\gamma) = \exp \boldsymbol{\alpha}_i$), as discussed in [1]. This ratio quantifies the relative difference in time it takes to achieve the pth percentile between two levels of a covariate. The pth percentile of the (covariate-adjusted) Weibull distribution occurs at

$$t_p = \left[\frac{-\log p}{\lambda e^{\boldsymbol{\beta}^T \mathbf{z}}} \right]^{1/\gamma}.$$

Then the ratio of times for a covariate with value z_1 versus values z_0, with parameter estimate β, can then be computed as:

$$\begin{aligned} \frac{t_B}{t_A} &= \left[\frac{-\log p}{\lambda e^{\boldsymbol{\beta} z_1}} \right]^{1/\gamma} \left[\frac{\lambda e^{\boldsymbol{\beta} z_0}}{-\log p} \right]^{1/\gamma} \\ &= \exp \left\{ \frac{\boldsymbol{\beta}(z_0 - z_1)}{\gamma} \right\}. \end{aligned}$$

Thus, if we are comparing treatment B to treatment A, where the parameter estimate for treatment B is $\boldsymbol{\beta}_{\text{trt}}$, then the ETR is $\exp\{-\boldsymbol{\beta}_{\text{trt}}/\gamma\}$.

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For example if the ETR for treatments A vs B is 1.2, then the amount of time it takes for p percent of patients with treatment A to have the event is predicted to be about 20% longer than it takes for the same percentage of patients with treatment B to experience an event. (That is, treatment B is worse.) For this reason, the ETR can also be called an "acceleration factor."

Additionally, a function `WeibullDiag` has been provided to check the adequacy of the Weibull Model.

1 `WeibullReg`

The `WeibullReg` function performs Weibull AFT regression on survival data, returning a list which contains:

formula the regression formula,

coef the coefficient table,

HR a table with the hazard rates (with confidence intervals) for each of the covariates,

ETR a table with the Event Time Ratios (with confidence intervals) for each of the covariates, and

summary the summary table from the original `survreg` model.

Such tables can also be produced using the `streg` function in `stata` with the following options: 1) the `nohr` option gives `coef`, 2) without any options gives `HR`, 3) the `tr` option gives `ETR`, and 4) the `time` option produces `summary`, the original output from `survreg`. While `proc lifereg` in SAS can also perform parametric regression for survival data, its output must also be transformed.

The following example reproduces Tables 12.1 and 12.2 from [2], on the larynx data set.

```
> library(survival)
> data(larynx)

> WeibullReg(Surv(time, death) ~ factor(stage) + age, data=larynx)

$formula
Surv(time, death) ~ factor(stage) + age

$coef
                 Estimate         SE
lambda         0.01853664 0.01898690
gamma          1.13014371 0.13844846
factor(stage)2 0.16692694 0.46112943
factor(stage)3 0.66289534 0.35550887
factor(stage)4 1.74502788 0.41476410
age            0.01973646 0.01424135

$HR
                     HR        LB        UB
factor(stage)2 1.181668 0.4786096  2.917491
```

```
factor(stage)3 1.940402 0.9666786  3.894946
factor(stage)4 5.726061 2.5398504 12.909334
age            1.019933 0.9918573  1.048802

$ETR
                     ETR        LB       UB
factor(stage)2 0.8626863 0.3880879 1.917678
factor(stage)3 0.5562383 0.2971113 1.041364
factor(stage)4 0.2135090 0.1047619 0.435140
age            0.9826879 0.9583820 1.007610

$summary

Call:
survival::survreg(formula = formula, data = data, dist = "weibull")
                 Value Std. Error     z       p
(Intercept)     3.5288     0.9041  3.90 9.5e-05
factor(stage)2 -0.1477     0.4076 -0.36   0.717
factor(stage)3 -0.5866     0.3199 -1.83   0.067
factor(stage)4 -1.5441     0.3633 -4.25 2.1e-05
age            -0.0175     0.0128 -1.37   0.172
Log(scale)     -0.1223     0.1225 -1.00   0.318

Scale= 0.885

Weibull distribution
Loglik(model)= -141.4   Loglik(intercept only)= -151.1
        Chisq= 19.37 on 4 degrees of freedom, p= 0.00066
Number of Newton-Raphson Iterations: 5
n= 90
```

The hazard rates produced with the Weibull regression model are similar to what is obtained with Cox proportional hazards regression:

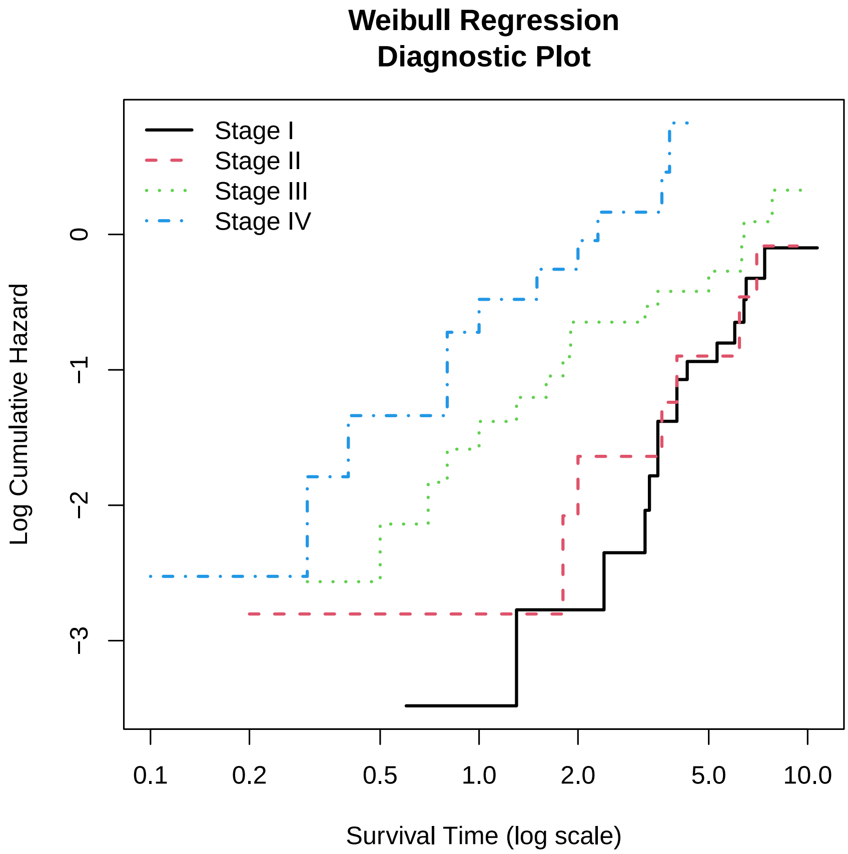
```
> cph <- coxph(Surv(time, death) ~ factor(stage) + age, data=larynx)
> summary(cph)$conf.int

               exp(coef) exp(-coef) lower .95 upper .95
factor(stage)2  1.150320  0.8693233 0.4646755  2.847656
factor(stage)3  1.901003  0.5260381 0.9459343  3.820364
factor(stage)4  5.506778  0.1815944 2.4085976 12.590147
age             1.019213  0.9811488 0.9911247  1.048098
```

Most of the work of the function is actually performed by `ConvertWeibull`. These functions require the `survival` package in R. Formulas for the variance estimates come from [2, Equations 12.2.13-18, with some modifications since R gives $\log\sigma$].

2 WeibullDiag

The `WeibullDiag` function produces a diagnostic plot for Weibull AFT regression, similar to what is in [2, Figure 12.2]. It plots $\log \text{Time}$ versus the log of the estimated cumulative hazard estimate. If the Weibull model has adequate fit, then the plots for each of the covariates should be roughly linear and parallel. This function requires the `survfit` object to contain `strata`, else an error is produced. The `WeibullDiag` function requires the `survival` package.

```
> WeibullDiag(Surv(time, death) ~ factor(stage), data = larynx,
+             labels=c("Stage I", "Stage II", "Stage III", "Stage IV"))
```



References

[1] K. J. Carroll. On the use and utility of the Weibull model in the analysis of survival data. *Controlled Clinical Trials*, 24(6):682 – 701, 2003.

[2] J. P. Klein and M. L. Moeschberger. *Survival Analysis: techniques for censored and truncated data*. Springer Verlag, 2003.