Weibull Regression with R, Part Two*

```
> rm(list=ls());  options(scipen=999)
> # install.packages("survival",dependencies=TRUE) # Only need to do this once
> library(survival) # Do this every time
> # install.packages("asaur",dependencies=TRUE) # Only need to do this once
> library(asaur)
> # help(pharmacoSmoking)
> head(pharmacoSmoking)
   id ttr relapse         grp age gender     race employment yearsSmoking
1  21 182       0   patchOnly  36   Male    white         ft           26
2 113  14       1   patchOnly  41   Male    white      other           27
3  39   5       1 combination  25 Female    white      other           12
4  80  16       1 combination  54   Male    white         ft           39
5  87   0       1 combination  45   Male    white      other           30
6  29 182       0 combination  43   Male hispanic         ft           30
  levelSmoking ageGroup2 ageGroup4 priorAttempts longestNoSmoke
1        heavy     21-49     35-49             0              0
2        heavy     21-49     35-49             3             90
3        heavy     21-49     21-34             3             21
4        heavy       50+     50-64             0              0
5        heavy     21-49     35-49             0              0
6        heavy     21-49     35-49             2           1825
> summary(pharmacoSmoking)
       id              ttr            relapse                grp    
 Min.   :  1.00   Min.   :  0.00   Min.   :0.000   combination:61  
 1st Qu.: 33.00   1st Qu.:  8.00   1st Qu.:0.000   patchOnly  :64  
 Median : 67.00   Median : 49.00   Median :1.000                   
 Mean   : 66.15   Mean   : 77.44   Mean   :0.712                   
 3rd Qu.: 99.00   3rd Qu.:182.00   3rd Qu.:1.000                   
 Max.   :130.00   Max.   :182.00   Max.   :1.000                   
      age            gender          race      employment  yearsSmoking  
 Min.   :22.00   Female:81   black   :38   ft   :72   Min.   : 9.00  
 1st Qu.:41.00   Male  :44   hispanic: 8   other:39   1st Qu.:22.00  
 Median :49.00               other   : 2   pt   :14   Median :30.00  
 Mean   :48.84               white   :77              Mean   :30.88  
 3rd Qu.:56.00                                        3rd Qu.:39.00  
 Max.   :86.00                                        Max.   :56.00  
 levelSmoking ageGroup2  ageGroup4  priorAttempts     longestNoSmoke 
 heavy:89     21-49:66   21-34:16   Min.   :   0.00   Min.   :   0.0  
 light:36     50+  :59   35-49:50   1st Qu.:   1.00   1st Qu.:   7.0  
                         50-64:48   Median :   2.00   Median :  90.0  
                         65+  :11   Mean   :  12.68   Mean   : 539.7  
                                    3rd Qu.:   5.00   3rd Qu.: 365.0  
                                    Max.   :1000.00   Max.   :6205.0  
> attach(pharmacoSmoking)
> 
> # Make patch only the reference category
> contrasts(grp) = contr.treatment(2,base=2)
> colnames(contrasts(grp)) = c('Combo') # Names of dummy vars -- just one
> DayOfRelapse = Surv(ttr+1,relapse) # Day of relapse starts with one.
> # Collapse race categories
> Race = as.character(race) # Small r race is a factor. This is easier to modify.
> Race[Race!='white'] = 'blackOther'; Race=factor(Race)
> table(race,Race)
          Race
race       blackOther white
  black            38     0
  hispanic          8     0
  other             2     0
  white             0    77
```

* Copyright information is on the last page.

```
> full = survreg(DayOfRelapse ~ grp + age + gender + Race + employment
+                              + yearsSmoking + levelSmoking + priorAttempts,
+                                dist='weibull')
> summary(full)

Call:
survreg(formula = DayOfRelapse ~ grp + age + gender + Race + 
    employment + yearsSmoking + levelSmoking + priorAttempts, 
    dist = "weibull")
                      Value Std. Error       z             p
(Intercept)         1.12177     0.9773  1.1479 0.25102045958
grpCombo            1.09225     0.3819  2.8603 0.00423234508
age                 0.08432     0.0341  2.4722 0.01342778276
genderMale          0.03631     0.4142  0.0877 0.93014517788
Racewhite           0.25145     0.3914  0.6424 0.52061740468
employmentother    -1.28799     0.4672 -2.7569 0.00583496922
employmentpt       -1.28482     0.5863 -2.1914 0.02842409501
yearsSmoking       -0.02351     0.0325 -0.7232 0.46955818306
levelSmokinglight -0.07347     0.4315 -0.1703 0.86480382316
priorAttempts      -0.00105     0.0020 -0.5244 0.59996899163
Log(scale)          0.54194     0.0892  6.0774 0.00000000122

Scale= 1.72 

Weibull distribution
Loglik(model)= -463.8   Loglik(intercept only)= -476.5
      Chisq= 25.41 on 9 degrees of freedom, p= 0.0025 
Number of Newton-Raphson Iterations: 5 
n= 125 

>
```

I am thinking about dropping Race, yearsSmoking, levelSmoking and priorAttempts. The last 3 variables all represent smoking history and could be correlated highly enough to wash out each other's effects. Test them simultaneously.

```
> 
> # Fit the restricted model: Restricted by H0
> rest1 =  survreg(DayOfRelapse ~ grp + age + gender + Race + employment ,
dist='weibull')
> anova(rest1,full) # LR test

Terms
1 grp + age + gender + Race + employment
2 grp + age + gender + Race + employment + yearsSmoking + levelSmoking + 
  priorAttempts
  Resid. Df    -2*LL Test Df  Deviance  Pr(>Chi)
1       117 928.3771      NA        NA        NA
2       114 927.5513    =  3 0.8258271 0.8432801
> 
> # Is Race significant with those variables dropped?
```

```
> # Is Race significant with those variables dropped?
> summary(rest1)

Call:
survreg(formula = DayOfRelapse ~ grp + age + gender + Race + 
    employment, dist = "weibull")
                  Value Std. Error      z           p
(Intercept)      1.3905     0.8684  1.601 0.10932864665
grpCombo         1.1021     0.3794  2.905 0.00367117788
age              0.0637     0.0190  3.354 0.00079527376
genderMale       0.0561     0.4140  0.136 0.89213377864
Racewhite        0.1880     0.3788  0.496 0.61958001498
employmentother -1.2821     0.4635 -2.766 0.00567301250
employmentpt    -1.2251     0.5837 -2.099 0.03582864119
Log(scale)       0.5444     0.0894  6.090 0.00000000113

Scale= 1.72 

Weibull distribution
Loglik(model)= -464.2   Loglik(intercept only)= -476.5
      Chisq= 24.58 on 6 degrees of freedom, p= 0.00041 
Number of Newton-Raphson Iterations: 5 
n= 125 
```

Decision: Drop race and gender.

```
> full2 =  survreg(DayOfRelapse ~ grp + age + employment , dist='weibull')
> summary(full2)

Call:
survreg(formula = DayOfRelapse ~ grp + age + employment, dist = "weibull")
                  Value Std. Error     z           p
(Intercept)      1.4957     0.8414  1.78 0.07545324261
grpCombo         1.1023     0.3793  2.91 0.00365915983
age              0.0643     0.0186  3.45 0.00055474131
employmentother -1.2880     0.4617 -2.79 0.00527676297
employmentpt    -1.2123     0.5616 -2.16 0.03088499029
Log(scale)       0.5454     0.0894  6.10 0.00000000105

Scale= 1.73 

Weibull distribution
Loglik(model)= -464.3   Loglik(intercept only)= -476.5
      Chisq= 24.31 on 4 degrees of freedom, p= 0.000069 
Number of Newton-Raphson Iterations: 5 
n= 125 

> 
> # Test employment status controlling for age and experimental treatment.
> rest2 = survreg(DayOfRelapse ~ grp + age , dist='weibull')
> anova(rest2,full2) # LR test
                   Terms Resid. Df    -2*LL Test Df Deviance    Pr(>Chi)
1              grp + age       121 937.9007      NA       NA          NA
2 grp + age + employment       119 928.6554    =  2 9.245333 0.009826558
> 
> # Test employment status with a Wald test.
> source("http://www.utstat.toronto.edu/~brunner/Rfunctions/Wtest.txt")
> # function(L,Tn,Vn,h=0) # H0: L theta = h
> # Tn is estimated theta, usually a vector.
> # Vn is the estimated asymptotic covariance matrix of Tn.
> # For Wald tests based on numerical MLEs, Tn = theta-hat,
> # and Vn is the inverse of the Hessian of the minus log
> # likelihood.
```

```
>
> Vhat = vcov(full2); Vhat
                 (Intercept)      grpCombo           age employmentother
(Intercept)      0.7079360800 -0.0320256900 -0.0147694486     0.111673731
grpCombo        -0.0320256900  0.1438698739 -0.0004703383    -0.013521493
age             -0.0147694486 -0.0004703383  0.0003472409    -0.003893727
employmentother  0.1116737308 -0.0135214927 -0.0038937268     0.213191081
employmentpt    -0.0003554818 -0.0078279548 -0.0013434899     0.077138486
Log(scale)      -0.0098224903  0.0050290739  0.0002048412    -0.003182291
                 employmentpt    Log(scale)
(Intercept)     -0.0003554818 -0.0098224903
grpCombo        -0.0078279548  0.0050290739
age             -0.0013434899  0.0002048412
employmentother  0.0771384860 -0.0031822913
employmentpt     0.3153999894 -0.0035442716
Log(scale)      -0.0035442716  0.0079888732

> thetahat = full2$coefficients; thetahat
    (Intercept)        grpCombo             age employmentother
      1.4957374       1.1023048       0.0643414      -1.2880472
   employmentpt
     -1.2122529
>
```

Note that the asymptotic covariance matrix includes log(sigma), but the "coefficients" vector does not.

```
> sigmahat = full2$scale; sigmahat
[1] 1.725305
> thetahat = c(thetahat,log(sigmahat))
>
> # H0: beta3=beta4=0. Express as H0: L theta = h
> eMat = rbind( c(0,0,0,1,0,0),
+               c(0,0,0,0,1,0)   )

> Wtest(L=eMat, Tn=thetahat, Vn=Vhat)
          W          df     p-value
9.718885315 2.000000000 0.007754805
> anova(rest2,full2) # Repeating LR test for comparison
                  Terms Resid. Df    -2*LL Test Df Deviance    Pr(>Chi)
1 grp + age                   121 937.9007      NA       NA          NA
2 grp + age + employment      119 928.6554    =  2 9.245333 0.009826558

>
> # Test part time versus other
> pto = cbind(0,0,0,1,-1,0); pto
     [,1] [,2] [,3] [,4] [,5] [,6]
[1,]    0    0    0    1   -1    0
> Wtest(L=pto, Tn=thetahat, Vn=Vhat)
         W          df    p-value
0.01534747 1.00000000 0.90140640
>
```

Predict the day of relapse for a 50 year old patient who is employed full time and gets the patch-only treatment.

Weibull Regression: $t_i = \exp\{\beta_0 + \beta_1 x_{i,1} + \ldots + \beta_{p-1} x_{i,p-1}\} \cdot \epsilon_i^\sigma = e^{\mathbf{x}_i^\top \boldsymbol{\beta}} \epsilon_i^\sigma$, where $\epsilon_1 \sim \exp(1)$.

- $t_i \sim$ Weibull, with $\alpha = 1/\sigma$ and $\lambda = e^{-\mathbf{x}_i^\top \boldsymbol{\beta}}$.
- $E(t_i) = e^{\mathbf{x}_i^\top \boldsymbol{\beta}} \Gamma(\sigma+1)$, $\text{Median}(t_i) = e^{\mathbf{x}_i^\top \boldsymbol{\beta}} \log(2)^\sigma$, $h_i(t) = \frac{1}{\sigma} \exp\{-\frac{1}{\sigma} \mathbf{x}_i^\top \boldsymbol{\beta}\} t^{\frac{1}{\sigma}-1}$.
- $S(t) = \exp\left\{-e^{-\frac{1}{\sigma}\mathbf{x}_i^\top \boldsymbol{\beta}} t^{\frac{1}{\sigma}}\right\}$

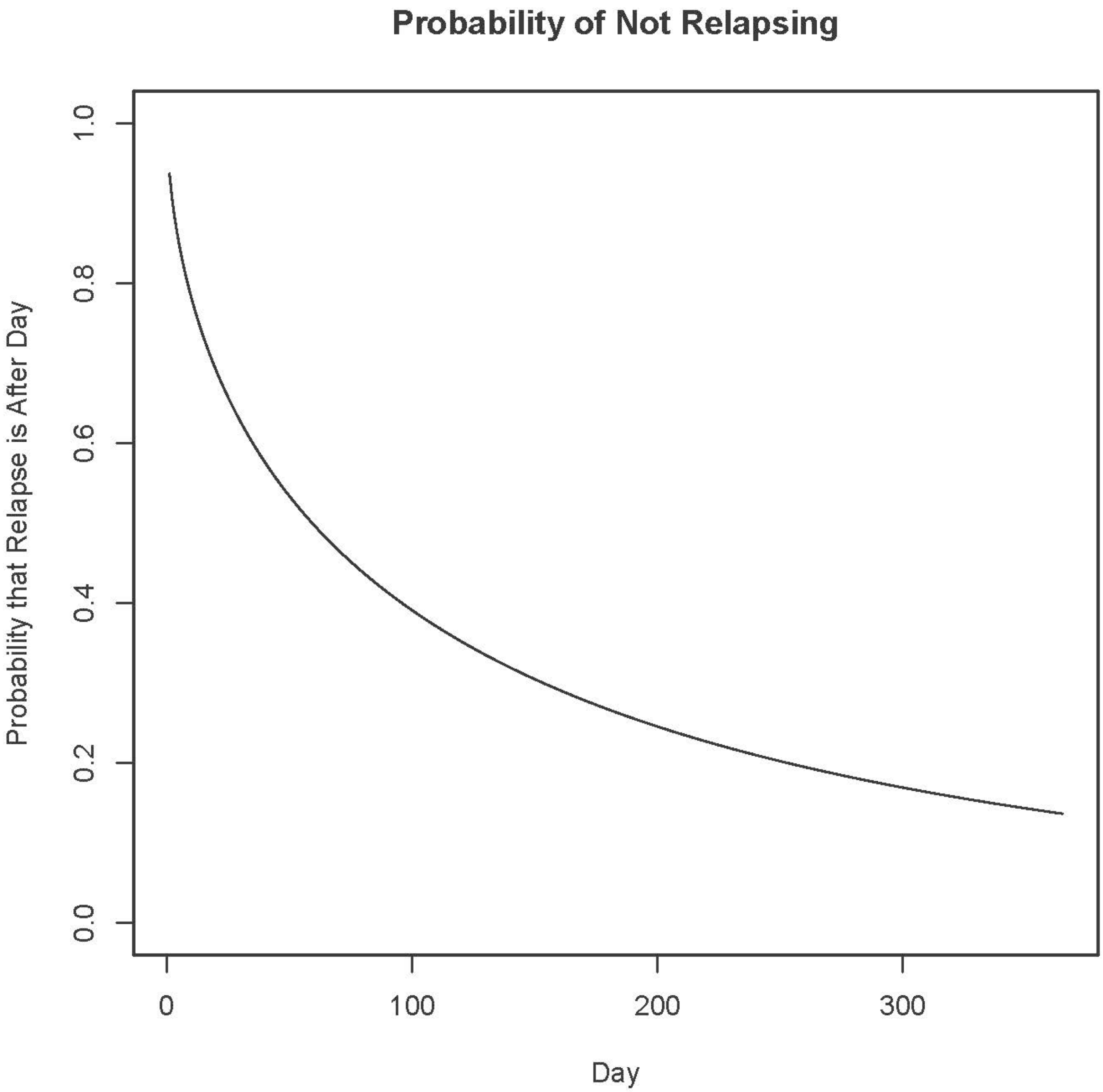
```
> thetahat
    (Intercept)         grpCombo              age employmentother 
      1.4957374        1.1023048        0.0643414      -1.2880472 
   employmentpt 
     -1.2122529        0.5454037 
> x = c(1,0,50,0,0,0)
> xb = sum(x*thetahat)
> 
> # a) Use the estimated mean
> exp(xb) * gamma(sigmahat+1)
[1] 175.5516
> 
> # b) Use the estimated median
> exp(xb) * log(2)^sigmahat
[1] 59.17273
> 
> # I think the median is preferable to mean because the Weibull distribution
> # is skewed. Also, the predict function for Weibull regression works as expected
> # for medians (but not means).
> 
> oldguy = data.frame(grp='patchOnly',age=50,employment='ft')
> predict(full2,newdata=oldguy,type='quantile',p=0.5,se=TRUE)
$fit
       1 
59.17273 

$se.fit
       1 
18.87577 

> # The 0.5 quantile is the median. se is from the delta method.
> 
> # Estimate and plot S(t) for the old guy.
```

The se is straightforward in theory, but messy in practice. G-dot from Mathematica is very ugly. For example, try `D[exp( - t^(1/s) exp( -(b0 + 50 b2)/s ),b0]`

```
> t = 1:365
> Shat = exp( -(exp(-xb/sigmahat)*t^(1/sigmahat)) )
> 
> plot(t,Shat,type='l',ylim=c(0,1),xlab='Day',
+ ylab='Probability that Relapse is After Day')
> title('Probability of Not Relapsing')
```

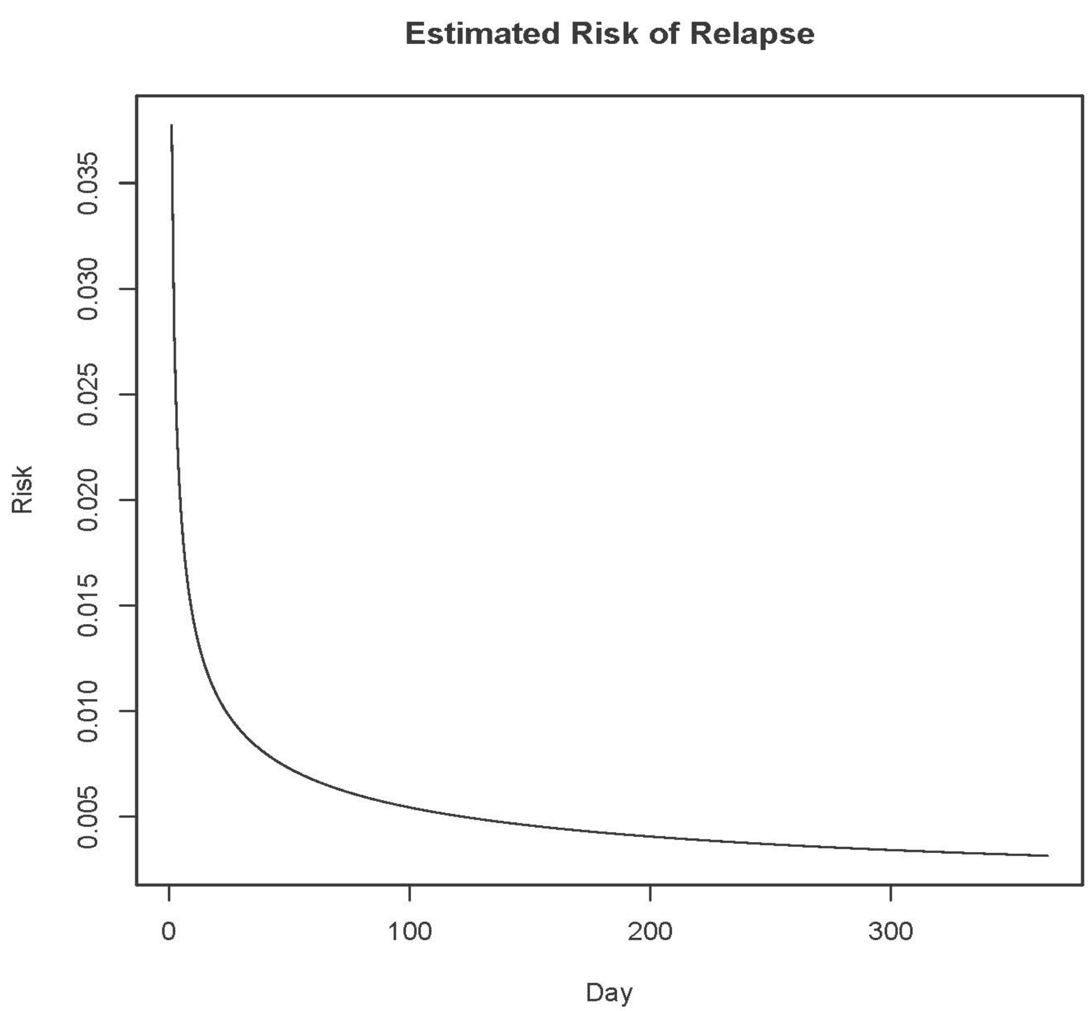


Probability of Not Relapsing
Probability that Relapse is After Day
0.0
0.2
0.4
0.6
0.8
1.0
0
100
200
300
Day

Plot estimated hazard function for that 50 year old patient who is employed full time and gets the patch-only treatment.

$$\begin{aligned} h(t) &= \frac{f(t)}{S(t)} \\ &= \frac{\alpha\lambda(\lambda t)^{\alpha-1}\, e^{-(\lambda t)^{\alpha}}}{e^{-(\lambda t)^{\alpha}}} \\ &= \alpha\lambda^{\alpha} t^{\alpha-1} \\ &= \frac{1}{\sigma} e^{-\frac{1}{\sigma}\mathbf{x}^{\top}\boldsymbol{\beta}}\, t^{\frac{1}{\sigma}-1} \end{aligned}$$

```
> h = 1/sigmahat * exp(-xb/sigmahat) * t^(1/sigmahat - 1)
> plot(t,h,type='l',xlab='Day',ylab='Risk',main='Estimated Risk of Relapse')
```



LaTeX code for the record

```
\noindent
Weibull Regression: $t_i = \exp\{\beta_0+\beta_1x_{i,1} + \ldots + \beta_{p-
1}x_{i,p-1} \} \cdot \epsilon_i^\sigma = e^{\mathbf{x}_i^\top
\boldsymbol{\beta}}\epsilon_i^\sigma$,
where $\epsilon_1 \sim \exp(1)$.
        \begin{itemize}
            \item $t_i \sim$ Weibull, with $\alpha = 1/\sigma$ and  $\lambda =
e^{-\mathbf{x}_i^\top \boldsymbol{\beta}}$.
            \item $E(t_i) = e^{\mathbf{x}_i^\top \boldsymbol{\beta}} \,
\Gamma(\sigma + 1)$,
                    Median($t_i$) = $e^{\mathbf{x}_i^\top \boldsymbol{\beta}} \,
\log(2)^\sigma$,
                    $h_i(t) = \frac{1}{\sigma} \exp\{-\frac{1}
{\sigma}\mathbf{x}_i^\top \boldsymbol{\beta}\}t^{\frac{1}{\sigma}-1}$.
           % \item[] $S(t) = e^{ -\left( e^{-\frac{1}{\sigma}\mathbf{x}_i^\top
\boldsymbol{\beta} } t^{\frac{1}{\sigma}} \right)}$
           \item $S(t) = \exp\left\{ - e^{-\frac{1}{\sigma}\mathbf{x}_i^\top
\boldsymbol{\beta} } t^{\frac{1}{\sigma}} \right\}   $
        \end{itemize}



% Hazard calculation

\begin{eqnarray*}
    h(t) & = & \frac{f(t)}{S(t)} \\
         & = & \frac{\alpha\lambda (\lambda t)^{\alpha-1} \, e^{-(\lambda
t)^\alpha}}
                    {e^{-(\lambda t)^\alpha}} \\
         & = & \alpha\lambda^\alpha t^{\alpha-1} \\
         & = & \frac{1}{\sigma} e^{-\frac{1}
{\sigma}\mathbf{x}^\top\boldsymbol{\beta}}
                      \,        t^{\frac{1}{\sigma} - 1}
\end{eqnarray*}
```