# Lecture fourteen: Parametric PH Models: The Weibull Model(I)

1. Population Survivor Distribution

   (a) The distribution of a population survival is often unknown.

   (b) Any theoritical distribution to approximate the true one?

   (c) Only few theoretical distributions available. Its use depends on

      i. How good the approximation is.

      ii. Mathematical tractability

   (d) Emperical distribution solely based on data, and it's non-parametric.

2. The strengths and limitations of parametric models (Therneau and Grambsch, 2000, pp. 28-31; JASA, 2004, vol. 99: 890-896)

   (a) Inferences will be more precise if the parametric assumption is valid.

   (b) Estimates tend to have smaller standard error (thus more efficient).

   (c) Few distributions available for parametric analysis, and difficulties in justification.

   (d) Bias when a wrong distribution is chosen.

3. Models for the hazard function
   $S(t)$, $h(t)$, $f(t)$ and $H(t)$ hold one-to-one relationship. See their relationships (formulas) derived in Section 1.4.

4. The exponential and Weibull distributions

   (a) **Exponential**

   Hazard function:

   $$h(t) = \lambda,$$

   for $0 \leq t < \infty$, $\lambda > 0$.

   Survival and density functions:

   $$S(t) = exp(-\lambda t),$$

and

$$f(t) = \lambda exp(-\lambda t),$$

Mean and the $p$th percentile ($S\{t(p)\} = 1 - (p/100)$):

$$E(T) = \frac{1}{\lambda}.$$

$$t(p) = \frac{1}{\lambda} log\,(\frac{100}{100-p}).$$

Memoryless property:

$$P(T > t_1 + t_0 | T > t_0) = exp\{-\lambda t_1\}.$$

The result means that conditional on survival to time $t_0$, the excess survival time beyond $t_0$ still has an exponential distribution with same parameter $\lambda$.

(b) **Weibull**

Hazard function:

$$h(t) = \lambda \gamma t^{\gamma-1},$$

for $0 \leq t < \infty$, $\lambda > 0$ and $\gamma > 0$.

Survival and density functions:

$$S(t) = exp(-\lambda t^{\gamma}),$$

$$f(t) = \lambda \gamma t^{\gamma-1} exp(-\lambda t^{\gamma}),$$

Mean and the $p$th percentile:

$$E(T) = \lambda^{-1/\gamma}\Gamma(\gamma^{-1}+1).$$

$$t(p) = [\frac{1}{\lambda} log\,(\frac{100}{100-p})]^{1/\gamma}.$$

(c) Figures: hazard and density for Weibull distribution

```
# Splus program generating the figures
weibull.s<-function(){
        sh <-c(3,1.5,0.5)
        med <- 20
        sc <- log(2)/med^sh
        t<- seq(0,45, by=0.5)
        f1<-sc[1]*sh[1]*t^(sh[1]-1)*exp(-sc[1]*t^sh[1])
        f2<-sc[2]*sh[2]*t^(sh[2]-1)*exp(-sc[2]*t^sh[2])
        f3<-sc[3]*sh[3]*t^(sh[3]-1)*exp(-sc[3]*t^sh[3])
        h1<-sc[1]*sh[1]*t^(sh[1]-1)
        h2<-sc[2]*sh[2]*t^(sh[2]-1)
        h3<-sc[3]*sh[3]*t^(sh[3]-1)
        motif()
        par(mfrow=c(2,2))
        plot(t, h1, xlab="Time", ylab="Hazard function",
                                          type="l",lty=1,lwd=1)
        lines(t, h2,lty=2,type="l",lwd=2)
        lines(t, h3,lty=3,type="l",lwd=2)
        legend(5,0.45,c("shape = 3","shape=1.5","shape=0.5"),
                                                cex=0.6,lty=1:3)
        plot(t, f1, xlab="Time", lty=1,lwd=1,type="l",
                           ylab="probability density function")
        lines(t, f2,lty=2,type="l",lwd=2)
        lines(t, f3,lty=3,type="l",lwd=2)
        text(t[50]+5, f1[50]-0.0025, "shape=3",cex=0.6)
        text(t[74]+4, f2[74]+0.0025, "shape=1.5",cex=0.6)
        text(t[34]+3, f3[34]+0.003, "shape=0.5",cex=0.6)
}
```

5. Assessing the suitability of a parametric model

Recall that exponential distribution is a special case of Weibull. For Weibull distribution,

$$log\{-log\, S(t)\} = log\, \lambda + \gamma log\, t.$$

(a) Example 5.1: IUD data

(b) The SAS program

```
options ls=80;
libname fu '../../sdata';
data w;
        set fu.iud;
filename gsasfile 'ex51a.gsf';
goptions reset=all gunit=pct border ftext=swissb htitle=6 htext=2.5
gaccess=gsasfile ROTATE=LANDSCAPE gsfmode=replace device=ps;
title1 'Log-cumulative hazard plot for IUD data';
symbol1 c=black i=join v=triangle height=3;

proc lifetest  notable plots=(lls) method=pl outsurv=a;
        time survt*censor(0);
data x1;
        set a;
        if survival=0 then delete;
        if survt = 0 then delete;
        ls=-log(survival);
        lls=log(-log(survival));
        logt=log(survt);
proc reg;
        model ls = survt/noint;
proc reg;
        model lls = logt;

filename gsasfile 'ex51b.gsf';
goptions reset=all gunit=pct border ftext=swissb htitle=6 htext=2.5
gaccess=gsasfile ROTATE=LANDSCAPE gsfmode=replace device=ps;
axis1 label=('survival time')
        width=2
        order=(10 to 107 by 15);
axis2 label=(a=90 'survival functions')
        width=2;
title1 'survival functions for IUD data';
footnote1 c=black f=special h=4 'L L'
        f=swiss h=4 ' exp'
        c=blue f=special h=3 '   m m '
```

```
        f=swissb h=4 ' Weibull';
symbol1 c=black i=join v=triangle height=3;
symbol2 c=blue i=join v=star height=3;
/* plug in parameters estimated from above regressions */
data x2;
        set x1;
        se=exp(-0.01021*survt);
        sw=exp(-exp(-6.3582)*(survt**(1.377252)));
proc gplot ;
        plot se*survt  sw*survt /overlay haxis=axis1 vaxis=axis2;
run;
```

(c) *The log-cumulative hazard plot*

6. Fitting a parametric model to a single sample

   The likelihood function:

$$L(\lambda, \gamma) = \prod_{i=1}^{r} f(t_{(i)}) \prod_{j=1}^{n-r} S(t_j^*) = \prod_{i=1}^{n} f^{\delta_i}(t_i) S^{1-\delta_i}(t_i)$$

   For log-likelihood function, score equations, and information matrix, MLE, see the second lecture notes for chapter 3.

   (a) Exponential distribution case

      i. without censoring

      ii. with censoring (what if no events?)

         follow the steps in the book at page 162-163

   (b) Example 5.3: IUD data (by hand and by sas program)

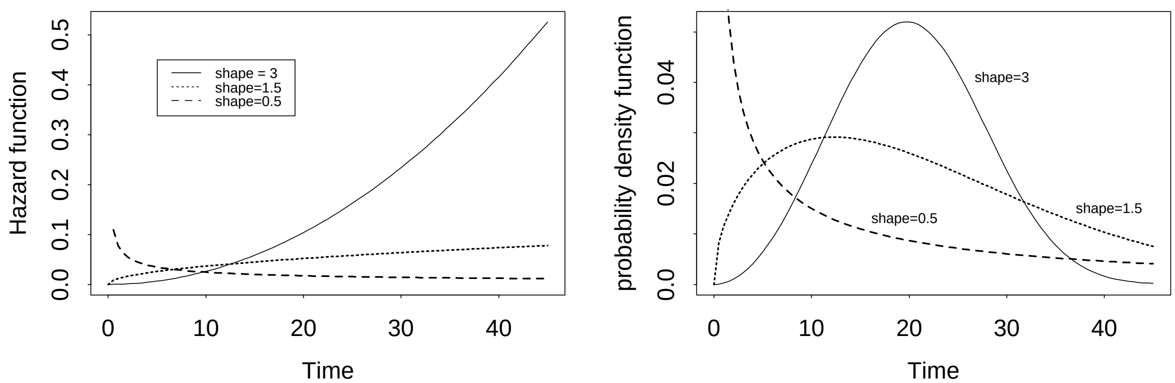
```
/* SAS program */
options ls=80;
libname fu '../../sdata';
data w;
        set fu.iud;
proc lifereg;
        model survt*censor(0) = / covb dist=exponential;
run;
```

```
/* SAS output */
       Analysis of Parameter Estimates

                          Standard   95% Confidence     Chi-
Parameter     DF Estimate    Error       Limits       Square Pr>ChiSq

Intercept      1   4.7555   0.3333   4.1022   5.4088  203.53   <.0001
Scale          0   1.0000   0.0000   1.0000   1.0000
Weibull Scale  1 116.2221  38.7407  60.4721 223.3688
Weibull Shape  0   1.0000   0.0000   1.0000   1.0000
```

(c) Weibull distribution case (one population)

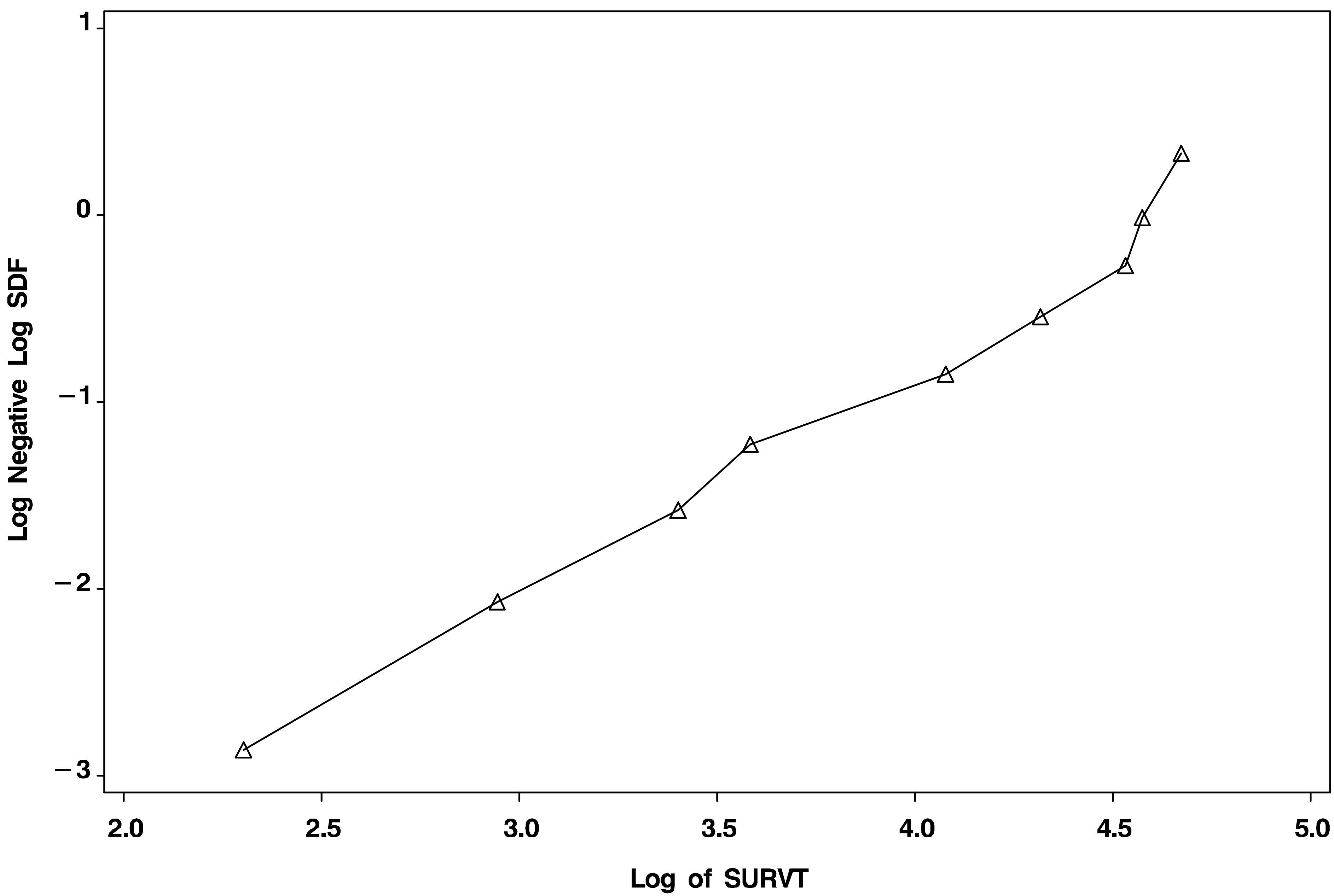
(d) Example 5.4: IUD data

Figure 1:



Hazard function
0.0
0.1
0.2
0.3
0.4
0.5
shape = 3
shape=1.5
shape=0.5
0
10
20
30
40
Time
probability density function
0.0
0.02
0.04
shape=3
shape=1.5
shape=0.5
Time

# Log-cumulative hazard plot for IUD data



# survival functions for IUD data