of parameters in these models. Throughout the literature on survival analysis, certain models have been used repeatedly; for example, exponential and Weibull models. Some others are gaining popularity; for example, log-logistic and Gompertz-Makeham models.

Some Survival Models

As before, $T$ is a random variable representing survival time, and $t > 0$ represents a typical point in this range. $S(t)$ and $\lambda(t)$ represent the survival and hazard functions of $T$, respectively. The exponential distribution is obtained by taking the hazard function to be a constant $\lambda$ over the range of $T$; the survival function is given by

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

An important generalization of the exponential distribution allows for a power dependence of the hazard on time. This yields the two-parameter Weibull distribution with hazard function

$$\lambda(t) = \lambda p(\lambda t)^{p-1}$$

for $\lambda, p > 0$. This hazard is monotone (decreasing for $p < 1$ and increasing for $p > 1$) and reduces to the exponential (constant) hazard if $p = 1$; $p$ is called the shape parameter.

We have the log-normal model when $Y = \log T$ is distributed as normal (Gaussian); this model is less convenient computationally because the survival and hazard functions do not have closed-form expressions. The hazard is not monotonic; it has value 0 at $t = 0$, increases to maximum and then decreases, approaching zero as $t$ becomes large—applications include chronic leukemia and Hodgkin’s disease. The log-logistic model is defined similarly with $Y$ having a logistic distribution.

The Gompertz model is another generalization of the exponential distribution, which allows for an exponential dependence of the hazard on time,

$$\lambda(t) = \alpha \exp(\beta t)$$
and the Gompertz-Makeham model adds an initial fixed component to the hazard function

\[ \lambda(t) = \lambda + \alpha \exp(\beta t) \]

We consider now a sample of survival data

\[ \{(t_i, \delta_i)\}_{i=1}^n \]

where \( t_i \) is the duration and \( \delta_i \) the survival status of the \( i \)th subject. Suppose that the survival model is specified up to one or several parameters \( \theta \) with the survival function \( S(t) \)

\[ S(t) = \Pr[T > t] \]

and density function \( f(t) \)

\[ f(t) \, dt = \Pr[t \leq T \leq t + dt] \]

As mentioned previously, an important feature of survival analysis is the need to accommodate right censoring in the data. Consider the case of random censorship and assume that the potential censoring time \( C_i \) for the \( i \)th subject is a random variable with survival and density functions \( R_i(t) \) and \( g_i(t) \) (see Chapter 1), respectively \( (i = 1, 2, \ldots, n) \), and further assume that \( C_i \)'s are stochastically independent of each other and of the survival times.

**Likelihood Function**

We now have

(i)

\[ \Pr[t_i \in (t,t + dt), \delta_i = 1] = \Pr[T_i \in (t,t + dt), C_i > t] \]

\[ = R_i(t)f(t)\, dt \]
Pr[t_i \in (t, t + dt), \delta_i = 0] = Pr[T_i > t, C_i \in (t, t + dt)]
= S(t)g_i(t)dt

Therefore, given the data \{(t_i, \delta_i)\}_{i=1}^n, the likelihood function is (up to a multiple constant)

\[ L = \prod_{i=1}^n [(R_i(t_i)f(t_i))^\delta_i[S(t_i)g_i(t_i)]^{1-\delta_i} \]
\[ = \prod_{i=1}^n [(R_i(t_i))^\delta_i[g_i(t_i)]^{1-\delta_i}] \{[f(t_i)]^\delta_i[S(t_i)]^{1-\delta_i} \}
\[ = \prod_{i=1}^n [(f(t_i))^\delta_i[S(t_i)]^{1-\delta_i} \text{ (up to a multiple constant)} \]
\[ = \prod_{i=1}^n [(\lambda(t_i))^\delta_iS(t_i) \]

because the term

\[ [R_i(t_i)]^\delta_i[g_i(t_i)]^{1-\delta_i} \]

does not involve the parameters of the survival model (this model specifies the distribution of T, which is independent from C, i.e., noninformative censoring).

**Exponential Model**

\[ L(\lambda) = \prod_{i=1}^n \lambda^\delta_ie^{-\lambda t_i} \]
\[ = \lambda^{\sum \delta_i}e^{-\lambda \sum t_i} \]
\[ = \lambda^d e^{-\lambda T} \]
where

\[ d = \sum_{i=1}^{n} \delta_i \]

= number of events

\[ T = \sum_{i=1}^{n} t_i \]

= total duration time

This leads to

\[ \ln L = d \ln \lambda - \lambda T \]

so that from

\[ 0 = \frac{d}{d\lambda} \ln L \]

\[ = \frac{d}{\lambda} - T \]

we have

\[ \hat{\lambda} = \frac{d}{T} \]

the usual rate frequently quoted in clinical research: deaths per treatment month (or person-year, etc.).

From

\[ -\frac{d^2}{d\lambda^2} \ln L = \frac{d}{\lambda^2} \]

the variance of \( \hat{\lambda} \) is given by

\[ \text{Var}(\hat{\lambda}) = \frac{\lambda^2}{E(d)} \]

There are three options for dealing with the denominator:
(i) Assume \( \{C_i\}_{i=1}^n \) are independent and identically distributed with certain survival function \( R(t) \) as in Chapter 1. This leads to

\[
E(d) = nE(\delta_i) = n \int_0^{\pi_2} R(t)f(t)\,dt
\]

For example, if \( C \) is distributed as uniform on \((\pi_2 - \pi_1, \pi_2)\) in a clinical trial, then

\[
E(d) = n \left\{ 1 - \frac{1}{\lambda \pi_1} [e^{-\lambda (\pi_2 - \pi_1)} - e^{-\lambda \pi_2}] \right\}
\]

(see the last part of Chapter 1).

(ii) Treat the potential censoring times \( \{C_i\}_{i=1}^n \) as fixed. The problem is for noncensored cases, \( C_i \)'s may be unknown in designs other than clinical trials. If we treat the \( C_i \)'s as fixed, then

\[
E(d) = \sum e - \lambda C_i
\]

(iii) The easiest way is to use observed information so that

\[
\text{Var}(\lambda) = 1^2 / d = d / T^2
\]

The 95% confidence interval for \( \lambda \), say, is given by

\[
\frac{d \pm 1.96 \sqrt{d}}{T}
\]

**Weibull Model**

We have

\[
L = \prod_{i=1}^{n} [\lambda \delta (\lambda t_i)^{p-1}] \delta \exp[-(\lambda t_i)^p]
\]