wish to incorporate measured covariates into the model. With covariates x measured at the time origin of the study, we can then think of models for the corresponding hazard function

$$\lambda(t;x) = \lim_{h \to 0} P\{T \in [t, t+h) | T \geq t, x\}/h,$$

which applies to those individuals with covariate value x. Corresponding to this, there are density and survivor functions, written $f(t;x)$ and $F(t;x)$, respectively.

1.3 TIME ORIGINS, CENSORING, AND TRUNCATION

In considering failure time data, it is important to have a clear and unambiguous definition of the time origin from which survival is measured. In some instances, time may represent age, with the time origin the birth of the individual. In other instances, the natural time origin may be the occurrence of some event, such as randomization or entry into a study or diagnosis of a particular disease. In like manner, one must have a clear definition of what constitutes failure. For example, in a trial to compare treatments of heart disease, one might take previous documented occurrence of a heart attack as providing eligibility for study. The time origin might be admission and randomization to the study, and failure may correspond to the recurrence of a heart attack. One would need to define carefully the clinical medical conditions that correspond to failure (and eligibility for the study). We will not talk about this further, but the clear identification of an origin and an endpoint are crucial applied aspects of failure time studies.

As noted earlier, failure time data often include some individuals who do not fail during their observation period; the data on these individuals are said to be *right censored*. In some situations, right censoring arises simply because some individuals are still surviving at the time that the study is terminated and the analysis is done. In other instances, individuals may move away from the study area for reasons unconnected with the failure time endpoint, so contact is lost. In yet other instances, individuals may be withdrawn or decide to withdraw from the study because of a worsening or improving prognosis. As is intuitively apparent, some censoring mechanisms have the potential to introduce bias into the estimation of survival probabilities or into treatment comparisons.

A right-censoring mechanism is said to be *independent* if the failure rates that apply to individuals on trial at each time $t > 0$ are the same as those that would have applied had there been no censoring. We discuss this idea more thoroughly in Chapter 6, but a brief discussion here is useful to set the stage. Suppose that the failure rate at time t that applies in the absence of censoring for an individual selected at random from a group with covariate value x is $\lambda(t;x)$. Here, as before, x consists of measurements taken on the individual at the time that he or she enters the study, such as age, sex, measures of physical condition, and so on. Suppose that within this group, individuals are to be censored according to a specific mechanism.

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Consider the subset of individuals who are at risk of failure (neither failed nor censored) at some time $t > 0$. The censoring mechanism or scheme is independent if for an individual selected at random from this subset, the failure rate is $\lambda(t;x)$. Thus we require that at each time t,

$$\lim_{h\to 0}\frac{P\{T\in[t,t+h)|x,T\geq t\}}{h}=\lim_{h\to 0}\frac{P\{T\in[t,t+h)|x,T\geq t,Y(t)=1\}}{h}, \qquad (1.9)$$

where $Y(t) = 1$ indicates that the individual has neither failed nor been censored prior to time t (is at risk of failure at time t). If the censoring scheme is independent, it can be shown that an individual who is censored at time t contributes the term $P(T > t;x) = F(t;x)$ to the likelihood. Thus the information that the individual is censored at time t tells us only that the time to failure exceeds t.

As mentioned, independent censoring is examined more fully in Chapter 6. It is interesting to note, however, that some standard censoring schemes are independent. Consider, for example, a random censorship model where the ith individual has a time T_i to failure and a time C_i to censoring. Given the covariate value x_i, we suppose that C_i and T_i are independent random variables. Further, conditional on the x_i's, (T_i, C_i) are independent, $i = 1, \ldots, n$, where n is the number of subjects in the study. The time T_i to failure is observed if $T_i \leq C_i$. Otherwise, the individual is censored at C_i. For this case, it is easy to see that

$$\lim_{h\to 0}\frac{P\{T_i\in[t,t+h)|x_i,T_i\geq t\}}{h}=\lim_{h\to 0}\frac{P\{T_i\in[t,t+h)|x_i,T_i\geq t,C_i\geq t\}}{h},$$

which is equivalent to the condition (1.9). Type II censoring, in which individuals are put on trial until the kth item fails, for some fixed k, was discussed briefly Section 1.1.4. This censoring scheme is also independent.

In general, a censoring scheme is independent if the probability of censoring at each time t depends only on the covariate x, the observed pattern of failures and censoring up to time t in the trial, or on random processes that are independent of the failure times in the trial. Mechanisms in which the failure times of individuals are censored because the individuals appear to be at unusually high (or low) risk of failure are not independent. For these mechanisms, the condition (1.9) is violated, and the basic methods of survival analysis are not valid. Because of this, it is very important to follow the individuals entered into a study as completely as possible, so that the possibility of dependent censoring is minimized.

In some studies, individuals are not identified for observation at their respective time origin, but rather, at the occurrence of a subsequent event. Thus, there is a larger group of individuals who could have been observed, but the study is comprised of a subset of those in the cohort who experience some intermediate event. For these individuals, we observe the time origin and the follow-up time until they fail or are censored. For example, suppose that is the chosen time variable, so that time of birth is the time origin. Interest centers on the group of individuals who

were exposed to some environmental risk, and individuals are identified for study at the time they respond to an advertisement. Any individuals who died prior to the advertisement are not observed, and in fact may not even be known to exist. Those who are observed are subject to *delayed entry* or *left truncation*. There is a condition similar to (1.9) for independent left truncation which requires that the failure rates of individuals under observation at time t are representative of those in the study population. Many of the methods and analyses that we discuss extend easily to allow for independent left truncation as well as independent right censoring.

Individuals can also be subject to *left censoring*, which occurs if the individual is observed to fail prior to some time t, but the actual time of failure is otherwise unknown. In this case, we observe that $T \in [0, t]$, which is analogous to right censoring, where we observe that $T \in (t, \infty)$. Left censoring should not be confused with left truncation, as discussed in the preceding paragraph. With left censoring, we know the individual exists and failed prior to the time t. With left truncation, the existence of an individual who fails before the beginning of observation is hidden from us.

Other types of censoring also arise. For example, in some situations individuals are interval censored, so we observe only that the failure time falls within some interval $T \in (a, b)$. One might also have situations in which individuals are subject to right truncation. That is, an individual is observed if and only if its failure time is less than some given time t. Exercise 1.13 gives an example. We discuss these more general censoring schemes in Chapter 3 in the context of parametric analyses. Most of our attention, however, is focused on independent right censoring and extensions to allow independent delayed entry or left truncation.

1.4 ESTIMATION OF THE SURVIVOR FUNCTION

1.4.1 Kaplan–Meier or Product Limit Estimator

The *empirical distribution function*,

$$\bar{F}_n(x) = \frac{\text{no. sample values} \leq x}{n}$$

is a simple estimate of the distribution function $\bar{F}(x) = P(X \leq x)$ and is a familiar and convenient way to summarize and display data. A plot of $\bar{F}_n(x)$ versus x visually represents the sample and provides full information on the percentile points, the dispersion, and the general features of the sample distribution. Besides these obvious descriptive uses, it is an indispensable aid in studying the distributional shape of the population from which the sample arose; in fact, the empirical distribution function can serve as a basic tool in constructing formal tests of goodness of fit of the data to hypothesized probability models (see, e.g., Cox and Hinkley, 1974, pp. 69ff.).

In the analysis of survival data, it is very often useful to summarize the survival experience of particular groups of patients in terms of the empirical survivor