## Chapter 1

# Introduction

It is universally recognized that lifetimes of individuals, components, systems, etc. are unpredictable and random, and hence amenable only to probabilistic and statistical laws. The development of models and methods to deal with such random variables took place in the second half of the twentieth century, although certain explicit and implicit results are from earlier times as well. The development proceeded in two main intermingling streams. The reliability theory stream is concerned with models for lifetimes of components and systems, in the engineering and industrial fields. The survival analysis stream mainly drew inspiration from medical and similar biological phenomena. In this book we bring the two streams together. Our aim is to emphasize the basic unity of the subject and yet to develop it in its diversity.

In all the diverse applications the random variable of interest is the time upto the occurrence of the specified event often called "death", "failure", "break down" etc. It is called the life time of the concerned unit. However, there are situations where the technical term "time" does not represent time in the literal sense. For example, it could be the number of operations a component performs before it breaks down. It could even be the amount that a health insurance company pays in a particular case.

**Examples of failure or life time situations:**

(1) A mechanical engineer conducts a fatigue test to determine the expected life of rods made of steel by subjecting $n$ specimens to an axial load that causes a specified stress. The number of cycles are recorded at the time of failure of every specimen.

(2) A manufacturer of end mill cutters introduces a new ceramic cutter material. In order to estimate the expected life of a cutter, the manufcturer places $n$ units under test and monitors the tool wear. A failure of the cutter occurs when the wear-out exceeds a predetermined value. Because of the budgeting constraints, the manufacturer runs the test for a month.

(3) A 72 hr. test was carried out on 25 gizmos, resulting in $r_1$ failure times (in hrs.). Of the remaining working gizmos on test $r_2$, were removed before the end of test duration (72 hrs) to satisfy customer demands. The rest were still working at the end of the 72 hr. test.

(4) *Leukemia patients* : Leukemia is cancer of blood and as in any other type of cancer, there are remission periods. In a remission period, the patient though not free of disease is free of symptoms. The length of the remission period is a variable of interest in this study. The patients in the state of remission are followed over time to see how long they stay in remission.

(5) *A prospective study of heart condition.* A disease free cohort of individuals is followed over several years to see who develops heart disease and when does it happen.

(6) *Recidivism study* : A recidivist is a person who relapses into crime. In this study, newly released parolees are followed in time to see whether and when they get rearrested for another crime.

(7) *Spring testing* : Springs are tested under cycles of repeated loading and failure time is the number of cycles leading to failure. Samples of springs are allocated to different stress levels to study the relationship between the lifetimes at different stress levels. At the lower stress levels failure times could be longer than at higher stress levels.

**Measurement of Survival Time (or Failure Time)**: Following points should be kept in mind while measuring the survival time. The time origin should be precisely defined for each individual. The individuals under study should be as similar as possible at their time origin. The time origin need *not* be and usually is *not* the same calender time for each individual. Most clinical trials have staggered entries, so that patients enter the study over a period of time. The survival time of a patient is measured from his/her own date of entry. Figure (1.1) and (1.2) show staggered entries and how these are aligned to have a common origin.

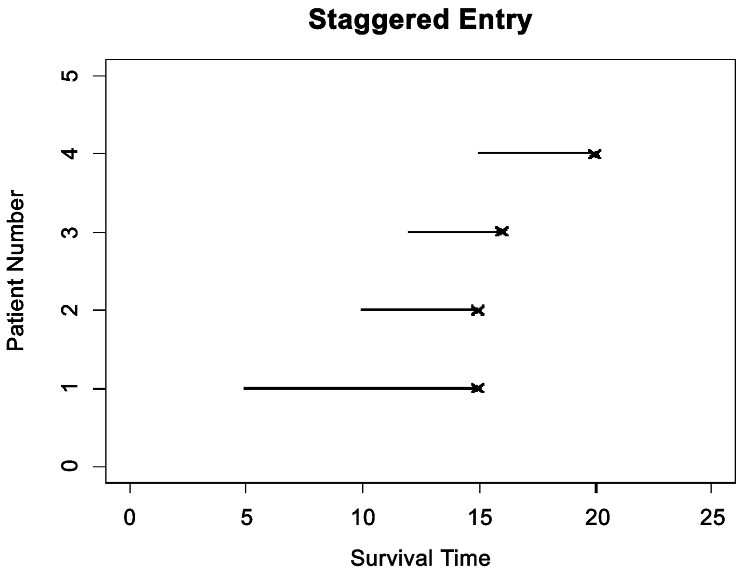


**Figure 1.1**

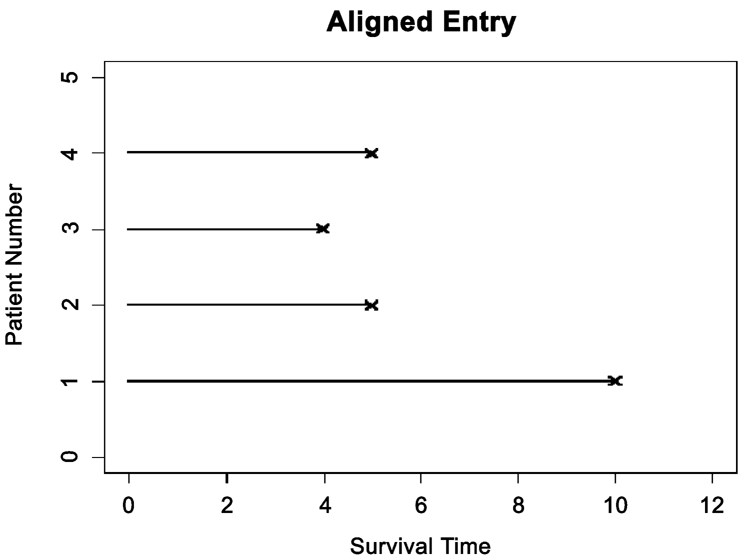


**Figure 1.2**

The concept of the point event of failure should be defined precisely. If a light bulb, for example, is operating continuously, then the number of hours for which it burned should be used as the life time. If the light bulb is turned on and off, as most are, the meaning of number of hours burned will be different as the shocks of lighting and putting off decreases the light bulb's life. This example indicates that there may be more to defining a lifetime than just the amount of time spent under operation.

**Censoring** : The techniques for reducing experimental time are known as censoring. In survival analysis the observations are lifetimes which can be indefinitely long. So quite often the experiment is so designed that the time required for collecting the data is reduced to manageable levels.

Two types of censoring are built into the design of the experiment to reduce the time taken for completing the study.

*Type I (Time Censoring)* : A number (say n) of identical items are simultaneously put into operation. However, the study is discontinued at a predetermined time $t_0$. Suppose $n_u$ items have failed by this time and the remaining $n_c = n - n_u$ items remain operative. These are called the censored items. Therefore the data consists of the lifetimes of the $n_u$ failed items and the censoring time $t_0$ for the remaining $n_c$ items. (see Figure 1.3).

*Example of type I censoring*

Power supplies are major units for most electronic products. Suppose a manufacturer conducts a reliability test in which 15 power supplies are operated over the same duration. The manufacturer decides to terminate the test after 80000 hrs. Suppose 10 power supplies fail during the fixed time interval. Then remaining five are type I censored.

*Type II (Order Censoring)* : Again a number (say n) of identical components are simultaneously put into operation. The study is discontinued when a predetermined number $k(< n)$ of the items fail. Hence the failure times of the $k$ failed items are available. These are the $k$ smallest order statistics of the complete random sample. For the remaining items the censoring time $x_{(k)}$, which is the failure time of the item failing last, is available. (See Figure 1.4.)

*Example of Type II censoring*

Twelve ceramic capacitors are subjected to a life test. In order to reduce the test time, the test is terminated after eight capacitors fail. The remaining are type II censored.

The above types of censoring are more prevalent in reliability studies (of engineering systems). In survival studies (of biomedical items) censoring is

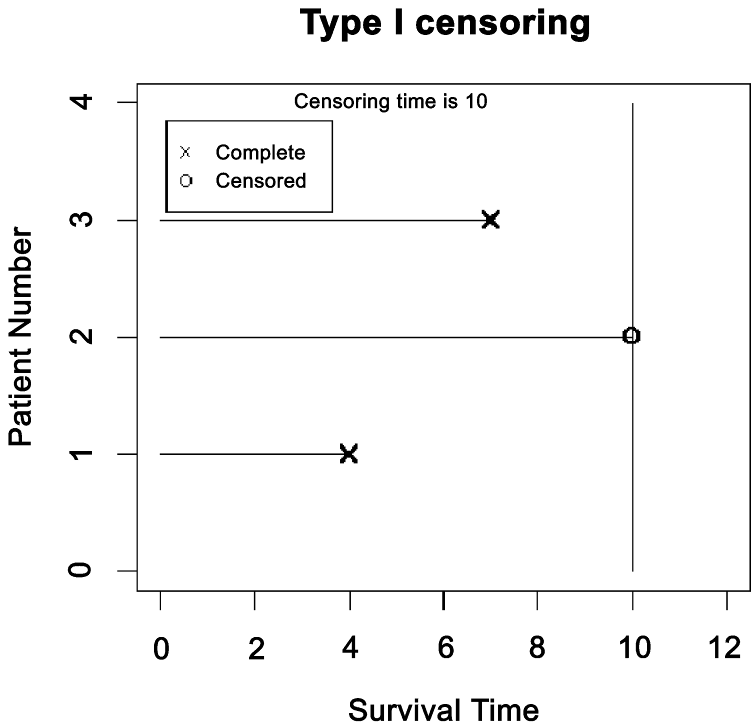


**Figure 1.3**

more a part of the experimental situation rather than a matter of deliberate design.

Undesigned censoring occurs when some information about individual survival time is available but exact survival time is *not* known. As a simple example of such undesigned censoring, consider leukemia patients who are followed until they go out of remission. If for a given patient, the study ends while the patient is still in remission (that is the event defining failure does not occur), then the patient's survival time is considered as censored. For this person, it is known that the survival time is not less than the period for which the person was observed. However, the complete survival time is *not* known.

The most frequent type of censoring is known as *right random censoring.* It occurs when the complete lifetimes are not observed for reasons which are beyond the control of the experimenter. For example, it may occur in any one of the following situations : (i) loss to follow-up; the patient

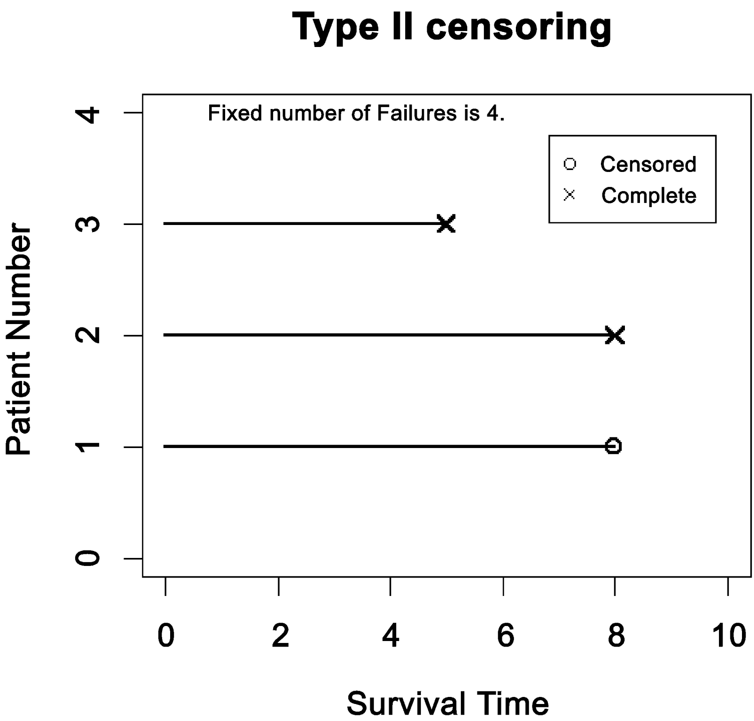


**Figure 1.4**

may decide to move elsewhere and therefore the experimenter may not see him/her again, (ii) withdrawal from the study; the therapy may have bad side effects so it may become necessary to discontinue the treatment or the patient may become non-cooperative, (iii) termination of the study; a person does not experience the event before the study ends. (iv) the value yielded by the unit under study may be outside the range of the measuring instrument, etc. Figure 1.5 illustrates a possible trial in which random censoring occurs. In this figure, patient 1 entered the study at $t = 0$ and died at $T = 5$, giving an uncensored observation. Patient 2 also entered the study at $t = 0$ and was still alive by the end of study, thus, giving a censored observation. Patient 3 has entered the study at $t = 0$ and lost to follow up before the end of study to give another censored observation.

*Example of Random (right) Censoring*

A mining company owns a 1,400 car fleet of 80 - ton high-side, rotary-dump gondolas. A car will accumulate about 100,000 miles per year. In

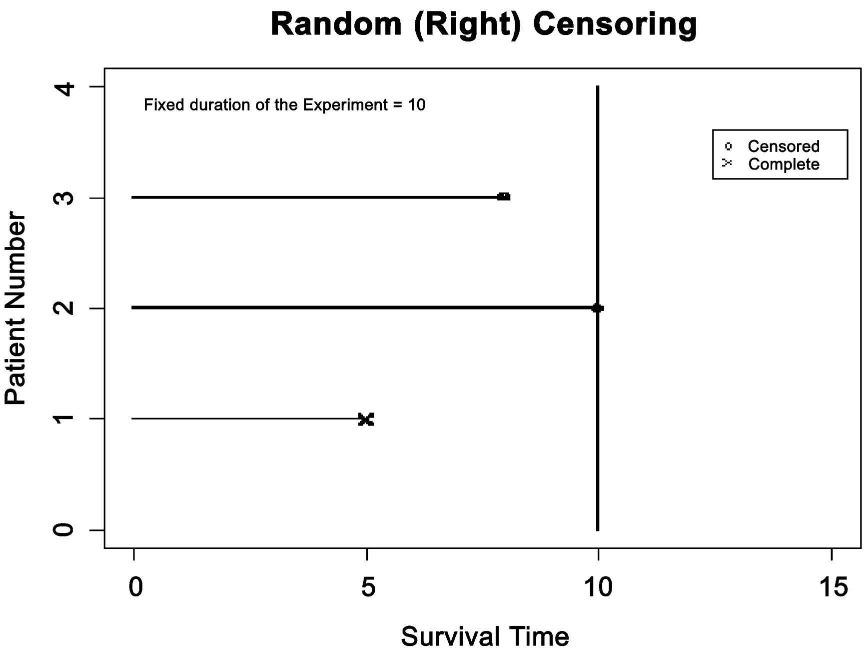


**Figure 1.5**

their travels from mines to a power plant, the cars are subjected to vibrations due to track input in addition to the dynamic effects of the longitudinal shocks coming through the couplers. As a consequence the couplers encounter high dynamic impacts and experience fatigue failure and wear. Twenty-eight cars are observed, and the miles driven until the coupler is broken are recroded. The remaining six cars left service after 151000, 155000, 160000, 168000, 175000 and 178000 miles. None of them experienced a broken coupler. Thus giving randomly right censored data.

It may be noted that in type I censoring the number of failures is a random variable whereas in type II censoring the time interval over which the observations are taken is a random variable. In random censoring, the number of complete (uncensored) observations is random and time for which the study lasts may also be random. The censoring time for every censored observation in type I and II censoring is identical, but not so in random censoring. Furthermore, type I censoring may be seen to be a particular case of random censoring by taking all censoring times equal to $t_0$.

Left censoring occurs less frequently than right censoring. It occurs when the observation (time for occurrence of the event) does not get recorded unless it is larger than a certain threshold which may or may not be identical for all observations. For example, the presence of certain gas cannot be measured unless it equals a threshold of six parts per million with a particular measuring device. Such data set will yield left-censored observations.

The data set may contain both left and right censored observations. A psychiatrist collected data to determine the age at which children have learned to perform a particular task. The lifetime was the time the child has taken to learn to perform the task from date of birth. Those children who already knew how to perform the task, when he arrived at the village were left censored and those who did not learn the task even by the time he departed were right-censored observations.

Interval censoring is still another type of censoring for which life time is known only to fall into an interval. This pattern occurs when the items are checked periodically for failure, when a recording instrument has lower as well as upper bounds on its measuring capacity etc. .

A simple minded approach to handling the problem of censoring is to ignore all censored values and to perform analysis only on those items that were observed to fail. However, this is not a valid approach. If, for example, this approach is used for right censored data, an overly pessimistic result concerning the mean of the lifetime distribution will result since the longer lifetimes were excluded from the analysis. The proper approach is to provide probabilistic models for the censoring mechanism also.

The second chapter entitled 'Ageing' actually is concerning the development of various mathematical models for the random variable of lifetime. We assume it to be a continuous, positive valued random variable. We make a case for the exponential distribution as the central probability distribution, rather than the normal distribution which is accorded this prime position in standard statistical theory. We discuss various properties of the exponential distribution. The notions of no-ageing and ageing rightly act as indicators while choosing the appropriate law. Positive ageing describes in many ways the phenomenon, that a unit which has already worked for some time has less residual lifetime left than a similar new unit, whereas negative ageing describes the opposite notion. This chapter concerns with many such weak and strong notions and defines nonparametric classes of probability distributions characterized by them. Starting with the exponential distribution as the sole no-ageing distribution we go on to define Increasing Failure Rate (IFR), Increasing Failure Rate Average (IFRA) and larger classes of distributions and their duals and discuss the properties of these classes. We also introduce the notion of a coherent system of components and show that the lifetime of such a system tends to have a distribution belonging to the IFRA class under fairly general positive aging conditions on the components. We round off this chapter by providing certain bounds for the unknown distributions belonging to the IFRA class in terms of the exponential distribution with the same value of a moment or of a quantile.

In Chapter 3 we go on to discuss many parametric families of probability distributions which are of special interest in life studies due to their ageing properties. These include direct generalizations of the exponential distribution such as the Weibull and the gamma families as well as Pareto and lognormal. We discuss the ageing and other properties and conclude with some notes on heuristic choice of a family for the experiment under consideration.

The fourth chapter deals with inference for the parameters of the distributions introduced in the previous chapter. We adopt the standard likelihood based frequentist inference procedures. As is well known, except for a few parametric models, the likelihood equations do not yield closed form solutions. In such cases one needs to obtain numerical solutions. These procedures too are described.

As explained above a distinguishing feature of data on lifetimes is the possibility of censored observations, either due to design or necessity. The realization that censored observations too are informative and should not be discarded is often seen by many as the true beginning of life data analysis. In the fourth chapter we present the modifications required in standard inference procedures in order to take care of censored data as well.

Beginning with the fourth chapter a distinctive feature of the book makes its appearance. It is data analysis on personal computers using R, a software system for statistical analysis and graphics created in the last decade. An introduction to R including reasons for its suitability and adoption are provided in the Appendix at the end of the book. In the fourth chapter we present the commands required for parametric analysis of data arising from exponential and other common life distributions.

In the fifth chapter we introduce nonparametric methods. The first problem to be tackled is that of estimating the distribution and the survival functions. Beginning with the empirical distribution function in the classical setting of complete observations, we go on to the Kaplan - Meier estimator to be used in the presence of randomly censored observations. In such functional estimation one has to appeal to methods of weak convergence or martingale and other stochastic processes based convergence. We therefore provide only indications of proofs of some results. We conclude the chapter with illustrations of R-based computations of the estimates and their standard errors.

The sixth chapter deals with tests of goodness of fit of the exponential distribution. In the context of life data it is important to decide whether the exponential model is appropriate, and if not, the direction of the possibly true alternative hypothesis. Since most of the statistics used for these tests are $U$-statistics (in the sense of Hoeffding) we devote the second section in this chapter to its development. A more complete development of $U$ - statistics may be found in books on Nonparametric Inference. Besides a number of analytic tests for exponentiality we also introduce certain graphical procedures based on the total time on test (TTT) transform. As in earlier chapters we illustrate these techniques through the R-software.

Next in the seventh chapter we deal with two sample nonparametric methods. We begin with an introductory section on two sample $U$-statistics and go on to discuss several tests for this problem. These include the Wilcoxon-Mann-Whitney (W-M-W) tests for location differences for complete samples. We discuss Gehan's modification of the W-M-W test for censored samples and further the Mantel-Haenszel, Tarone - Ware classes of statistics and the long-rank test of Peto and Peto. It is our experience that the Kaplan-Meier estimation of the survival function and the Mantel - Haenszel two sample tests are the two most frequently included methods of life data analysis in general statistical softwares. In this as in the previous chapter we provide the R-commands for the application of these two procedures.

We proceed to regression problems in Chapter 8. In classical statistical inference regression is discussed as the effect of covariates on the means of the random variables, or in the case of dichotomous variables, on the log odds ratio. Cox (1972), in a path breaking contribution, suggested that the effects of the covariates on the failure rate are relevant in life time studies. He developed a particularly appealing and easy to administer model in terms of effects of covariates which are independent of the age of the subject. This model is called the proportional hazards model. It is a semiparametric model in terms of a baseline hazard rate (which may be known or unknown) and a link function of regression parameters which connect the values of the covariates to it. We provide standard methodology for estimating these parameters and testing hypotheses regarding them in case of complete or censored observations. R-commands to carry out these procedures are also provided.

The ninth chapter too considers a problem which was first considered in the setting of life time studies. The failure of a unit, when it occurs, may be ascribed to one of many competing risks. Hence the competing risks data consists of $(T, \delta)$, the time to failure $(T)$ as well as the cause of failure $(\delta)$. Later on this model was extended to any situation which looked at the time of occurrence of a multinomial event along with the event that occured, as the basic data. We discuss both parametric and nonparametric methodology for such data, pointing out the non-identifiability difficulties which arise in the case of dependent risks.

So far we have discussed the problems of statistical inference in the classical setting of a random sample consisting of independent and identically distributed random variables, sometimes subject to censoring. In the tenth chapter we consider repairable systems which upon failure are repaired and made operational once more. The data is then in the form of a stochastic process. The degree of repair is an issue. We consider the minimal repair discipline which specifies that the system after repair is restored to the operational state and is equivalent to what it was just prior to failure. The nonhomogeneous Poisson process (NHPP) is seen to be an appropriate model in this context. We discuss estimation of parameters as well as certain tests in this context in this chapter. Certain R-commands are provided for fitting a piecewise constant intensity function to such data.

We conclude the book with an Appendix which introduces statistical analysis using R. The basic methodology including its installation, methods of data input, carrying out the required analysis and other necessary information is provided here.