

## Statistics Notes

## Survival probabilities (the Kaplan-Meier method)

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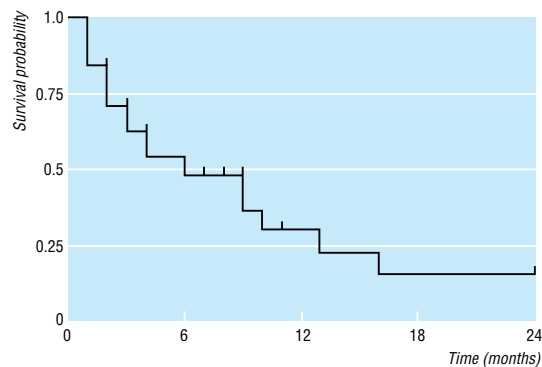
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As we have observed,<sup>1</sup> analysis of survival data requires special techniques because some observations are censored as the event of interest has not occurred for all patients. For example, when patients are recruited over two years one recruited at the end of the study may be alive at one year follow up, whereas one recruited at the start may have died after two years. The patient who died has a longer observed survival than the one who still survives and whose ultimate survival time is unknown.

The table shows data from a study of conception in subfertile women.<sup>2</sup> The event is conception, and women "survived" until they conceived. One woman conceived after 16 months (menstrual cycles), whereas several were followed for shorter time periods during which they did not conceive; their time to conceive was thus censored.

We wish to estimate the proportion surviving (not having conceived) by any given time, which is also the estimated probability of survival to that time for a member of the population from which the sample is drawn. Because of the censoring we use the Kaplan-Meier method. For each time interval we estimate the probability that those who have survived to the beginning will survive to the end. This is a conditional probability (the probability of being a survivor at the end of the interval on condition that the subject was a survivor at the beginning of the interval). Survival to any time point is calculated as the product of the conditional probabilities of surviving each time interval. These data are unusual in representing months (menstrual cycles); usually the conditional probabilities relate to days. The calculations are simplified by ignoring times at which there were no recorded survival times (whether events or censored times).

In the example, the probability of surviving for two months is the probability of surviving the first month times the probability of surviving the second month given that the first month was survived. Of 38 women, 32 survived the first month, or 0.842. Of the 32 women at the start of the second month ("at risk" of conception), 27 had not conceived by the end of the month. The conditional probability of surviving the second month is thus  $27/32 = 0.844$ , and the overall probability of surviving (not conceiving) after two months is  $0.842 \times 0.844 = 0.711$ . We continue in this way to the end of the table, or until we reach the last event. Observations censored at a given time affect the number still at risk at the start of the next month. The estimated probability changes only in months when there is a conception. In practice, a computer is used to do these calculations. Standard errors and confidence intervals for the estimated survival probabilities can be found by Greenwood's method.<sup>3</sup> Survival probabilities are usually presented as a survival curve (figure). The "curve" is a step function, with sudden changes in the estimated probability corresponding to times at which an event was observed. The times of the censored data are indicated by short vertical lines.



Survival curve showing probability of not conceiving among 38 subfertile women after laparoscopy and hydrotubation<sup>2</sup>

There are three assumptions in the above. Firstly, we assume that at any time patients who are censored have the same survival prospects as those who continue to be followed. This assumption is not easily testable. Censoring may be for various reasons. In the conception study some women had received hormone treatment to promote ovulation, and others had stopped trying to conceive. Thus they were no longer part of the population we wanted to study, and their survival times were censored. In most studies some subjects drop out for reasons unrelated to the condition under study (for example, emigration). If, however, for some patients in this study censoring was related to failure to conceive this would have biased the estimated survival probabilities downwards.

Secondly, we assume that the survival probabilities are the same for subjects recruited early and late in the study. In a long term observational study of patients with cancer, for example, the case mix may change over the period of recruitment, or there may be an innovation in ancillary treatment. This assumption may be tested, provided we have enough data to estimate survival curves for different subsets of the data.

Thirdly, we assume that the event happens at the time specified. This is not a problem for the conception data, but could be, for example, if the event were recurrence of a tumour which would be detected at a regular examination. All we would know is that the event happened between two examinations. This imprecision would bias the survival probabilities upwards. When the observations are at regular intervals this can be allowed for quite easily, using the actuarial method.<sup>3</sup>

Formal methods are needed for testing hypotheses about survival in two or more groups. We shall describe the logrank test for comparing curves and the more complex Cox regression model in future Notes.

1 Altman DG, Bland JM. Time to event (survival) data. *BMJ* 1997;317:468-9.

2 Luthra P, Bland JM, Stanton SL. Incidence of pregnancy after laparoscopy and hydrotubation. *BMJ* 1982;284:1013-4.

3 Parmar MKB, Machin D. *Survival analysis: a practical approach*. Chichester: Wiley, 37, 47-9.

Time (months) to  
conception or  
censoring in 38  
sub-fertile women  
after laparoscopy  
and hydrotubation<sup>2</sup>

Conceived	Did not conceive
1	2
1	3
1	4
1	7
1	7
1	8
2	8
2	9
2	9
2	9
2	11
3	24
3	24
3	
4	
4	
4	
6	
6	
9	
9	
9	
10	
13	
16	