# Chapter 47
# Interval Censored Data Analysis for Assessing Mean Time to Cancer Relapse (51 Patients)

## General Purpose

In survival studies often time to first outpatient clinic check instead of time to event is measured. Somewhere in the interval between the last and current visit an event may have taken place. For simplicity such data are often analyzed using the proportional hazard model of Cox (Chap. 17, Cox regression, pp. 209–212, in: Statistics applied to clinical studies 5th edition, Springer Heidelberg Germany, 2012, from the same authors). However, this analysis is not entirely appropriate. It assumes that time to first outpatient check is equal to time to relapse. However, instead of a time to relapse an interval is given, in which the relapse has occurred, and so this variable is somewhat more loose than the usual variable time to event. An appropriate statistic for the current variable would be the mean time to relapse inferenced from a generalized linear model with an interval censored link function, rather than the proportional hazard method of Cox.

## Primary Scientific Question

This chapter is to assess whether an appropriate statistic for the variable "time to first check" in survival studies would be the mean time to relapse, as inferenced from a generalized linear model with an interval censored link function.

## Example

In 51 patients in remission their status at the time-to-first-outpatient-clinic-control was checked (mths = months).

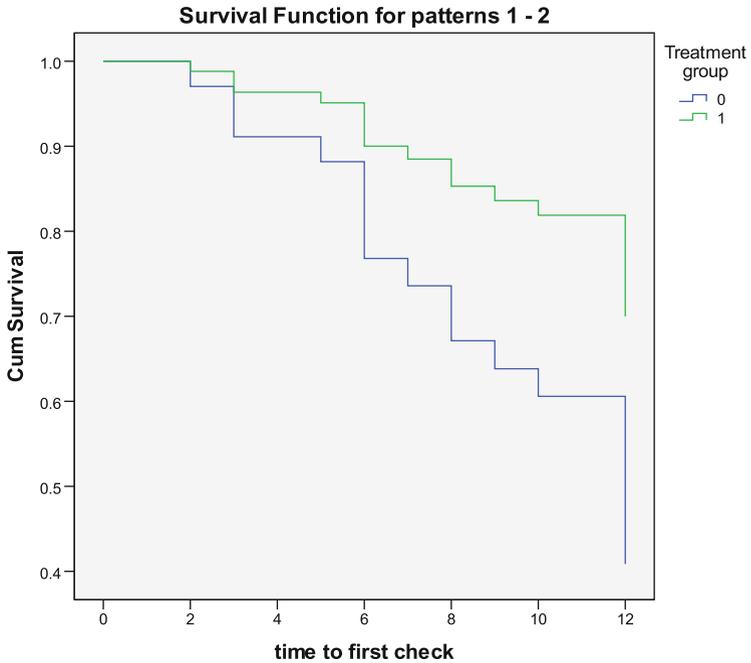| treatment (0 and 1) | time to first check (mths) | result (0 = remission 1 = relapse) |
|---|---|---|
| 1 | 11 | 0 |
| 0 | 12 | 1 |
| 0 | 9 | 1 |
| 1 | 12 | 0 |
| 0 | 12 | 0 |
| 1 | 12 | 0 |
| 1 | 5 | 1 |
| 1 | 12 | 0 |
| 1 | 12 | 0 |
| 0 | 12 | 0 |

The first 10 patients are above. The entire data file is entitled "intervalcensored. sav", and is in extras.springer.com. Cox regression was applied. Start by opening the data file in SPSS statistical software.

**Command:**

Analyze….Survival….Cox Regression….Time : time to first check….Status : result….Define Event….Single value: type 1….click Continue….Covariates: enter treatment….click Categorical….Categorical Covariates: enter treatment….click Continue….click Plots….mark Survival….Separate Lines for: enter treatment…. click Continue….click OK.

| Variables in the Equation | | | | | | |
|---|---|---|---|---|---|---|
| | B | SE | Wald | df | Sig. | Exp(B) |
| Treatment | .919 | .477 | 3.720 | 1 | .054 | 2.507 |

Example                                                                                    291


Survival Function for patterns 1 - 2

The above table is in the output. It shows that treatment is not a significant predictor for relapse. In spite of the above Kaplan-Meier curves, suggesting the opposite, the treatments are not significantly different from one another because p>0.05. However, the analysis so far is not entirely appropriate. It assumes that time to first outpatient check is equal to time to relapse. However, instead of a time to relapse an interval is given between 2 and 12 months in which the relapse has occurred, and so this variables is somewhat more loose than the usual variable time to event. An appropriate statistic for the current variable would be the mean time to relapse inferenced from a generalized linear model with an interval censored link function, rather than the proportional hazard method of Cox.

**Command:**

Analyze….click Generalized Linear Models….click once again Generalized Linear Models….Type of Model….mark Interval censored survival….click Response…. Dependent Variable: enter Result….Scale Weight Variable: enter "time to first check"….click Predictors….Factors: enter "treatment"….click Model….click once again Model: enter once again "treatment"….click Save….mark Predicted value of mean of response….click OK.

Parameter estimates

| Parameter | B | Std. Error | 95 % Wald confidence interval | | Hypothesis test | | |
| | | | Lower | Upper | Wald Chi-Square | df | Sig. |
|---|---|---|---|---|---|---|---|
| (Intercept) | .467 | .0735 | .323 | .611 | 40.431 | 1 | .000 |
| [treatments] | −.728 | .1230 | −.969 | −.487 | 35.006 | 1 | .000 |
| [treatments] | 0ᵃ | | | | | | |
| (Scale) | 1ᵇ | | | | | | |

Dependent Variable: Result
Model: (Intercept), treatment
ᵃSet to zero because this parameter Is redundant
ᵇFixed at the displayed value

The generalized linear model shows, that, after censoring the intervals, the treatment 0 is, compared to treat 1, a very significant better maintainer of remission. When we return to the data, we will observe as a novel variable, the mean predicted probabilities of persistent remission for each patient. This is shown underneath for the first 10 patients. For the patients on treatment 1 it equals 79,7 %, for the patients on treatment 0 it is only 53,7 %. And so, treatment 1 performs, indeed, a lot better than does treatment 0 (mths = months).

| treatment (0 and 1) | time to first check (mths) | result (0 = remission) | Mean Predicted_ 1 1 = relapse) |
|---|---|---|---|
| 1 | 11 | 0 | .797 |
| 0 | 12 | 1 | .537 |
| 0 | 9 | 1 | .537 |
| 1 | 12 | 0 | .797 |
| 0 | 12 | 0 | .537 |
| 1 | 12 | 0 | .797 |
| 1 | 5 | 1 | .797 |
| 1 | 12 | 0 | .797 |
| 1 | 12 | 0 | .797 |
| 0 | 12 | 0 | .537 |

# Conclusion

This chapter assesses whether an appropriate statistic for the variable "time to first check" in survival studies is the mean time to relapse, as inferenced from a generalized linear model with an interval censored link function. The current example shows that, in addition, more sensitivity of testing is obtained with p-values of 0.054

versus 0.0001. Also, predicted probabilities of persistent remission or risk of relapse for different treatment modalities are given. This method is an important tool for analyzing such data.

## Note

More background, theoretical and mathematical information of survival analyses is given in Chap. 17, Cox regression, pp. 209–212, in: Statistics applied to clinical studies 5th edition, Springer Heidelberg Germany, 2012, from the same authors.