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stcp-marshall-survival

Survival Analysis

Survival analysis is concerned with data where we measure the time to some event and the outcome of interest is the time to an event. Commonly the event is death (hence the name survival analysis), but it can be other outcomes.

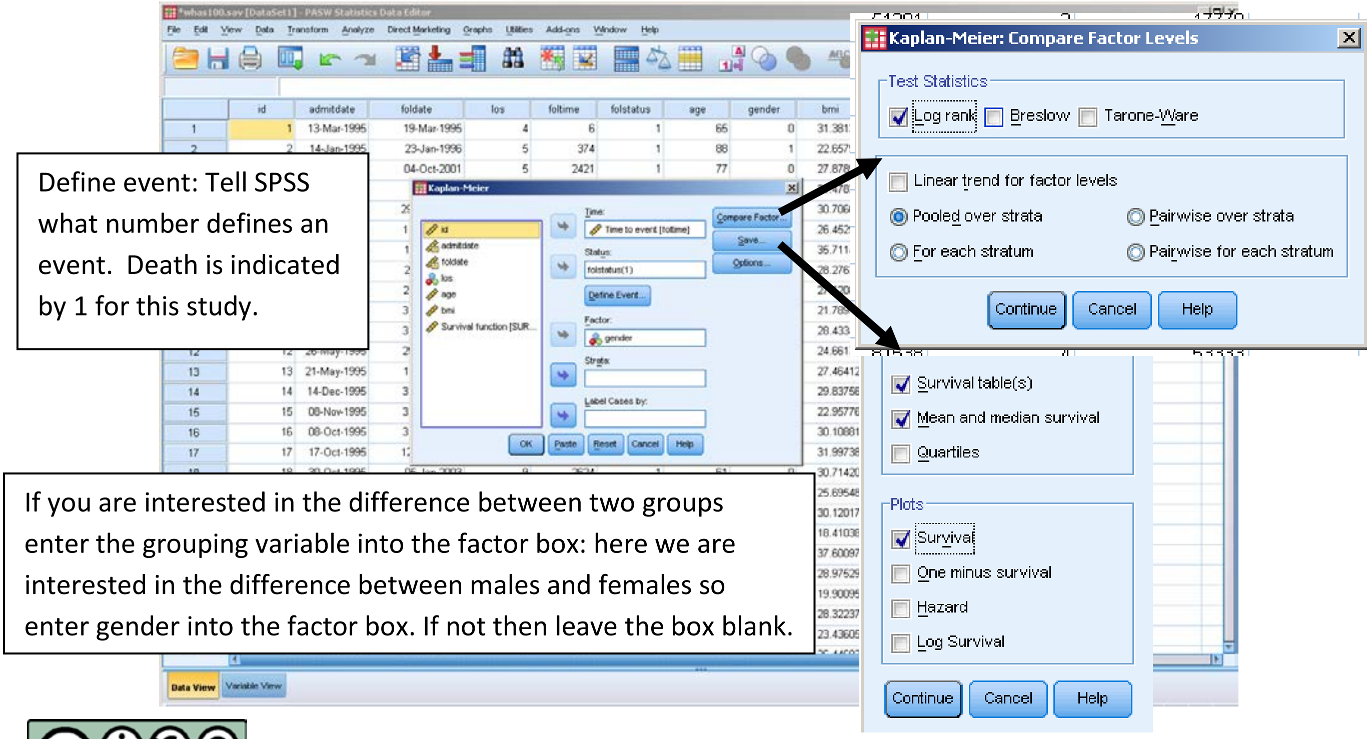
DATA: Worcester Heart Attack Study data from Dr. Robert J. Goldberg of the Department of Cardiology at the University of Massachusetts Medical School

DESCRIPTIVE ABSTRACT: The main goal of this study is to describe factors associated with trends over time in the incidence and survival rates following hospital admission for acute myocardial infarction (MI). Data have been collected during thirteen 1-year periods beginning in 1975 and extending through 2001 on all MI patients admitted to hospitals in the Worcester, Massachusetts Standard Metropolitan Statistical Area.

Producing a Kaplan-Meier Plot

A Kaplan-Meier plot displays survivals curves (cumulative probability of an individual remaining alive/ disease free etc. during a unit of time). Note: The cumulative survival probability is the product of the survival probabilities up to that point in time.

ANALYSE → SURVIVAL → KAPLAN-MEIER and select the following options:



Define event: Tell SPSS what number defines an event. Death is indicated by 1 for this study.

If you are interested in the difference between two groups enter the grouping variable into the factor box: here we are interested in the difference between males and females so enter gender into the factor box. If not then leave the box blank.

Kaplan-Meier

Time: Time to event [foltime]

Status: folstatus(1)

Factor: gender

Kaplan-Meier: Compare Factor Levels

Test Statistics

☑ Log rank ☐ Breslow ☐ Tarone-Ware

☐ Linear trend for factor levels

● Pooled over strata ○ Pairwise over strata

○ For each stratum ○ Pairwise for each stratum

☑ Survival table(s)

☑ Mean and median survival

☐ Quartiles

Plots

☑ Survival

☐ One minus survival

☐ Hazard

☐ Log Survival

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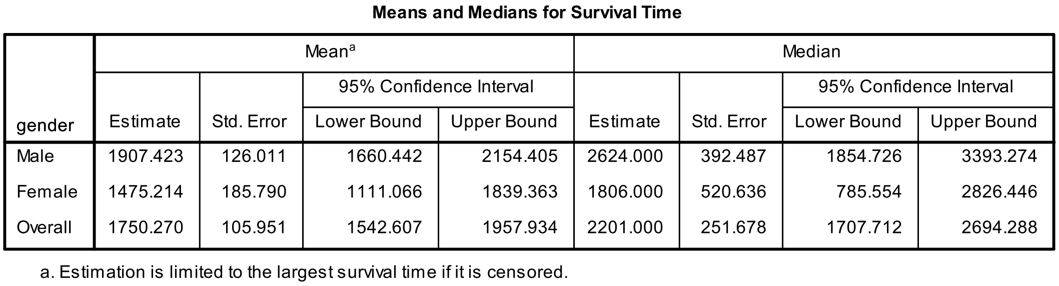
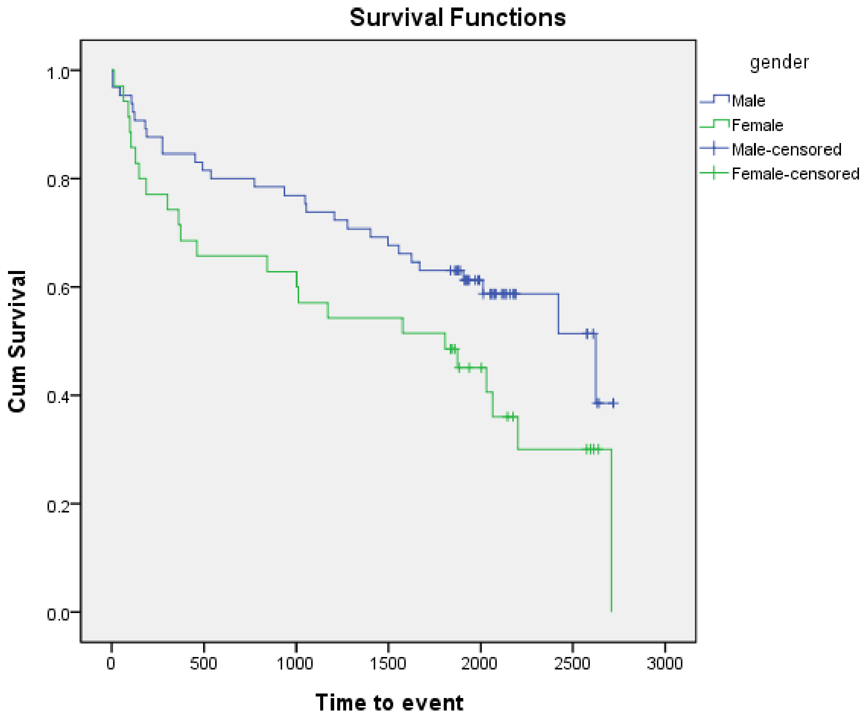
Summary statistics for the two groups: survival times should be summarised using the median time to event (shown in the following figure). Estimated time until death is 2624 days for males and 1806 days for females following admission for acute myocardial infarction.



Means and Medians for Survival Time

gender	Mean[a]				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
Male	1907.423	126.011	1660.442	2154.405	2624.000	392.487	1854.726	3393.274
Female	1475.214	185.790	1111.066	1839.363	1806.000	520.636	785.554	2826.446
Overall	1750.270	105.951	1542.607	1957.934	2201.000	251.678	1707.712	2694.288

a. Estimation is limited to the largest survival time if it is censored.



The Kaplan-Meier plot shows that the survival probability is lower for females at all time points so they are less likely to survive. Censoring means that an individual is still alive at the end of the study or that they withdrew from the study at that point in time.

The Log Rank Test

The log-rank test investigates the hypothesis that there is no difference in survival times between the groups studied. The log rank test compares the observed and expected number of events for each group using the same test statistic as the chi-squared test.

Estimation of the Test Statistic for comparing two groups A and B: $\chi^2_{logrank} = \frac{(O_A - E_A)^2}{E_A} + \frac{(O_B - E_B)^2}{E_B}$

Where the expected number of events is calculated as: $E_{Aj} = \sum \frac{d_j n_{Aj}}{n_j}$

d_j = no. of events at time t_j, n_{Aj} = no. of people at risk at time j in group A and n_j = total no. of people at risk.

Calculating the expected values is time consuming and the estimation of the test statistic is conservative. Instead you can use SPSS to calculate the test statistic and significance value.

Compare the test statistic with the critical value from the Chi-squared table. The degrees of freedom are: number of groups – 1 so for a significance level of 5% and 1 df, the critical value is $\chi^2_1 = 3.84$. If the test statistic is larger than 3.84, reject the null hypothesis and conclude that there is significant evidence to suggest a difference in survival times for the two groups.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	3.971	1	.046

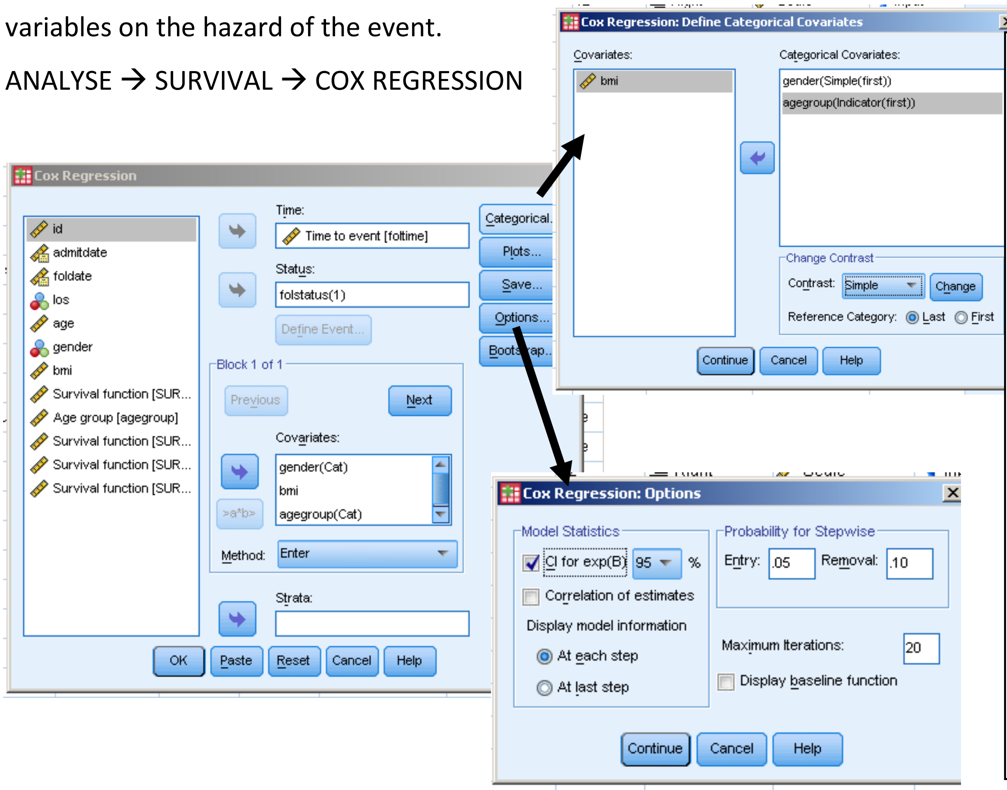
Test of equality of survival distributions for the different levels of gender.

The p-value (sig) is the probability of getting a test statistic of at least 3.971 if there really is no difference in survival times for males and females. As the p-value = 0.046 and is less than 0.05, conclude that there is significant evidence of a difference in survival times for males and females. The estimated time until death is 2624 days for males and 1806 days for females this difference is statistically significant (p=0.046) therefore, males have an increased survival time compared to females following admission to hospital due to myocardial infarction.

Cox's Regression

Cox's regression allows several variables to be taken into account and tests the independent effects of these variables on the hazard of the event.

ANALYSE → SURVIVAL → COX REGRESSION



Cox Regression

Variables: id, admitdate, foldate, los, age, gender, bmi, Survival function [SUR..., Age group [agegroup], Survival function [SUR..., Survival function [SUR..., Survival function [SUR...

Time: Time to event [foltime]

Status: folstatus(1)

Block 1 of 1

Covariates: gender(Cat), bmi, agegroup(Cat)

Method: Enter

Strata:

Cox Regression: Define Categorical Covariates

Covariates: bmi

Categorical Covariates: gender(Simple(first)), agegroup(Indicator(first))

Change Contrast

Contrast: Simple

Reference Category: ● Last ○ First

Cox Regression: Options

Model Statistics

☑ CI for exp(B): 95 %

□ Correlation of estimates

Display model information

● At each step

○ At last step

Probability for Stepwise

Entry: .05 Removal: .10

Maximum Iterations: 20

□ Display baseline function

For all categorical variables, select the 'Categorical' option. Tell SPSS whether you want to compare factor levels to the first or last category and select the 'Simple' option (although indicator appears to give the same main output). Click on change after each variable. Look at the help for info on other options but stick with simple for now.

For gender, selecting the reference category as first means that males are the reference category (as male = 0, female =1).

Hazard = the risk of reaching the event (e.g. death) at time point i, given that the individual has not reached it up to that time point, t. A lower hazard rate implies a higher survival rate. If the outcome is death the hazard rate can be interpreted as the mortality rate.

Model: $\lambda_i(t) = \lambda_0(t)\exp(\beta_1 x_1 + \beta_2 x_2 + \ldots. + \beta_k x_k)$ where:

There's a lot of output from SPSS but the following table contains the important output.

$\lambda_i(t)$ = the hazard function at time point t for individual I,

$\lambda_0(t)$ = the baseline hazard function (hazard function when all explanatory variables are set to 0)

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
gender	.183	.309	.352	1	.553	1.201	.655	2.203
bmi	-.071	.036	3.860	1	.049	.931	.867	1.000
agegroup			7.333	3	.062			
agegroup(1)	.103	.522	.039	1	.844	1.108	.399	3.081
agegroup(2)	.906	.457	3.940	1	.047	2.475	1.012	6.058
agegroup(3)	1.010	.453	4.978	1	.026	2.745	1.131	6.665

To understand the effects of individual predictors, look at Exp(β), which is the hazard ratio and can be interpreted as the predicted change in the hazard for a unit increase in the predictor.

What's a Hazard Ratio?

$$HR = \frac{h_A(t)}{h_B(t)} = \frac{risk\ of\ event\ (e.g.death)\ in\ group\ A}{risk\ of\ event\ in\ group\ B}$$

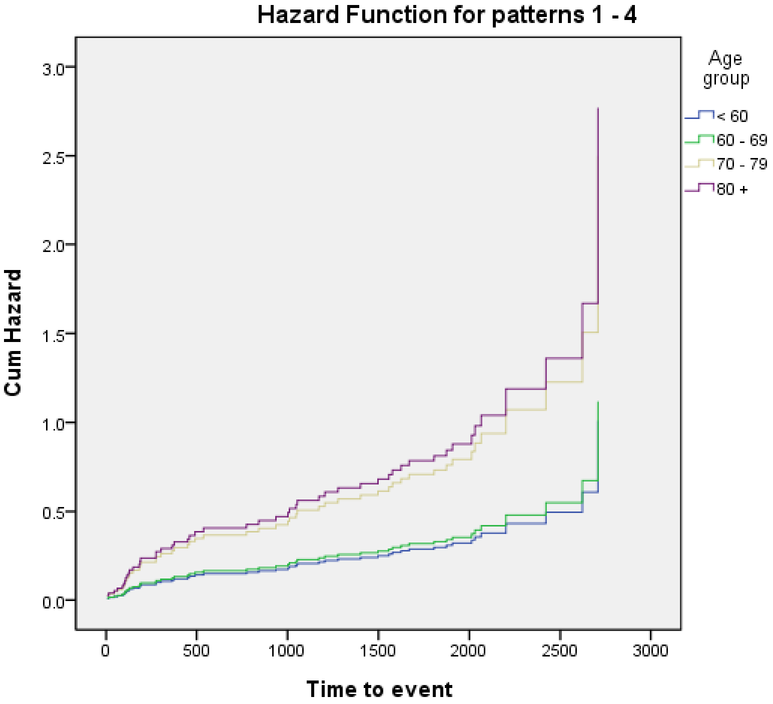
A hazard ratio can be interpreted in a similar way to relative risk. It compares the risk of an event occurring in two groups. If the ratio is above 1, the risk of the event happening in group A is higher.

For gender, the reference category was males so the hazard ratio is $\frac{h_{females}(t)}{h_{males}(t)}$ = 1.201. This indicates that the hazard (mortality) rate is 20% higher for females compared to males although the p-value and CI suggest this could be due to chance i.e. is non-significant.

The effect of BMI is statistically significant. For each additional unit of BMI, the hazard decreases by (1 – 0.931)*100 = 6.9%. For an additional 5 units increase in BMI, the hazard decreases by (1 – 0.931^5)*100 = 30%

For age group, the reference category is < 60. The next category is 60 – 69, then 70 – 79 and lastly 80+. For categorical variables, interpret Exp(β) directly e.g. the hazard (mortality) rate for 70 – 79 year olds is 147.5% higher than that of under 60's. The hazard (mortality) rate is 174.5% higher for the patients in the 80+ age group compared to those in the under 60's age group.

Assumptions



There is one main assumption for survival analysis that is particularly important for Cox's regression. This is the proportional hazards assumption that the hazard ratio between two groups remains constant over time. Requesting a hazard plot in the cox regression menu gives you a figure like the one opposite. The lines should not cross each other and should be approximately parallel. If this is not the case modelling survival based on a distribution should be considered instead.

The proportional hazards assumption also applies to the log rank test and can be checked by assessing if the lines on the Kaplan-Meier plot remain parallel. If this assumption is violated the log-rank test has reduced power, in extreme cases it is an appropriate test to use.