Chapter 565

Cox Regression

Introduction

This procedure performs Cox (proportional hazards) regression analysis, which models the relationship between a set of one or more covariates and the hazard rate. Covariates may be discrete or continuous. Cox's proportional hazards regression model is solved using the method of marginal likelihood outlined in Kalbfleisch (1980).

This routine can be used to study the impact of various factors on survival. You may be interested in the impact of diet, age, amount of exercise, and amount of sleep on the survival time after an individual has been diagnosed with a certain disease such as cancer. Under normal conditions, the obvious statistical tool to study the relationship between a response variable (survival time) and several explanatory variables would be multiple regression. Unfortunately, because of the special nature of survival data, multiple regression is not appropriate. Survival data usually contain censored data and the distribution of survival times is often highly skewed. These two problems invalidate the use of multiple regression. Many alternative regression methods have been suggested. The most popular method is the proportional hazard regression method developed by Cox (1972). Another method, Weibull regression, is available in **NCSS** in the Distribution Regression procedure.

Further Reading

Several books provide in depth coverage of Cox regression. These books assume a familiarity with basic statistical theory, especially with regression analysis. Collett (1994) provides a comprehensive introduction to the subject. Hosmer and Lemeshow (1999) is almost completely devoted to this subject. Therneau and Grambsch (2000) provide a complete and up-to-date discussion of this subject. We found their discussion of residual analysis very useful. Klein and Moeschberger (1997) provides a very readable account of survival analysis in general and includes a lucid account of Cox regression.

The Cox Regression Model

Survival analysis refers to the analysis of elapsed time. The response variable is the time between a *time origin* and an *end point*. The end point is either the occurrence of the event of interest, referred to as a *death* or *failure*, or the end of the subject's participation in the study. These elapsed times have two properties that invalidate standard statistical techniques, such as t-tests, analysis of variance, and multiple regression. First of all, the time values are often positively skewed. Standard statistical techniques require that the data be normally distributed. Although this skewness could be corrected with a transformation, it is easier to adopt a more realistic data distribution.

The second problem with survival data is that part of the data are *censored*. An observation is censored when the end point has not been reached when the subject is removed from study. This may be because the study ended before the subject's response occurred, or because the subject withdrew from active participation. This may be because the subject died for another reason, because the subject moved, or because the subject quit following the study protocol. All that is known is that the response of interest did not occur while the subject was being studied.

When analyzing survival data, two functions are of fundamental interest—the *survivor function* and the *hazard function*. Let T be the survival time. That is, T is the elapsed time from the beginning point, such as diagnosis of cancer, and death due to that disease. The values of T can be thought of as having a *probability distribution*.

Cox Regression

Suppose the *probability density function* of the random variable *T* is given by $f(T)$. The *probability distribution function* of *T* is then given by

$$\begin{aligned} F(T) &= \Pr_{T}(t < T) \\ &= \int_0 f(t)\mathrm{d}t \end{aligned}$$

The *survivor function*, $S(T)$, is the probability that an individual survives past *T*. This leads to

$$\begin{aligned} S(T) &= \Pr(T \geq t) \\ &= 1 - F(T) \end{aligned}$$

The *hazard function* is the probability that a subject experiences the event of interest (death, relapse, etc.) during a small time interval given that the individual has survived up to the beginning of that interval. The mathematical expression for the hazard function is

$$\begin{aligned} h(T) &= \lim_{\Delta T \to 0} \frac{\Pr(T \leq t < (T + \Delta T) \mid T \leq t)}{\Delta T} \\ &= \lim_{\Delta T \to 0} \frac{F(T + \Delta T) - F(T)}{\Delta T} \\ &= \frac{f(T)}{S(T)} \end{aligned}$$

The cumulative hazard function $H(T)$ is the sum of the individual hazard rates from time zero to time *T*. The formula for the cumulative hazard function is

$$H(T) = \int_0^T h(u)du$$

Thus, the hazard function is the derivative, or slope, of the cumulative hazard function. The cumulative hazard function is related to the cumulative survival function by the expression

$$S(T) = e^{-H(T)}$$

or

$$H(T) = -\ln(S(T))$$

We see that the distribution function, the hazard function, and the survival function are mathematically related. As a matter of convenience and practicality, the hazard function is used in the basic regression model.

Cox (1972) expressed the relationship between the hazard rate and a set of covariates using the model

$$\ln[h(T)] = \ln[h_0(T)] + \sum_{i=1}^{p} x_i \beta_i$$

or

$$h(T) = h_0(T) e^{\sum_{i=1}^{p} x_i \beta_i}$$

where $x_1, x_2, \cdots, x_p$ are covariates, $\beta_1, \beta_2, \cdots, \beta_p$ are regression coefficients to be estimated, *T* is the elapsed time, and $h_0(T)$ is the baseline hazard rate when all covariates are equal to zero. Thus the linear form of the regression model is

$$\ln\left[\frac{h(T)}{h_0(T)}\right] = \sum_{i=1}^{p} x_i \beta_i$$

Taking the exponential of both sides of the above equation, we see that this is the ratio between the actual hazard rate and the baseline hazard rate, sometimes called the *relative risk*. This can be rearranged to give the model

$$\begin{aligned}\frac{h(T)}{h_0(T)} &= \exp\left(\sum_{i=1}^{p} x_i\beta_i\right) \\ &= e^{x_1\beta_1}e^{x_2\beta_2}\cdots e^{x_p\beta_p}\end{aligned}$$

The regression coefficients can thus be interpreted as the relative risk when the value of the covariate is increased by one unit.

Note that unlike most regression models, this model does not include an intercept term. This is because if an intercept term were included, it would become part of $h_0(T)$.

Also note that the above model does not include *T* on the right-hand side. That is, the relative risk is constant for all time values. This is why the method is called *proportional hazards*.

An interesting attribute of this model is that you only need to use the ranks of the failure times to estimate the regression coefficients. The actual failure times are not used except to generate the ranks. Thus, you will achieve the same regression coefficient estimates regardless of whether you enter the time values in days, months, or years.

Cumulative Hazard

Under the proportional hazards regression model, the cumulative hazard is

$$\begin{aligned}H(T,X) &= \int_0^T h(u,X)du \\ &= \int_0^T h_0(u)e^{\sum_{i=1}^{p} x_i\beta_i}du \\ &= e^{\sum_{i=1}^{p} x_i\beta_i}\int_0^T h_0(u)du \\ &= H_0(T)e^{\sum_{i=1}^{p} x_i\beta_i}\end{aligned}$$

Note that the survival time *T* is present in $H_0(T)$, but not in $e^{\sum_{i=1}^{p} x_i\beta_i}$. Hence, the cumulative hazard up to time *T* is represented in this model by a baseline cumulative hazard $H_0(T)$ which is adjusted by the covariates by multiplying by the factor $e^{\sum_{i=1}^{p} x_i\beta_i}$.

Cumulative Survival

Under the proportional hazards regression model, the cumulative survival is

$$\begin{aligned}S(T,X) &= \exp(-H(T,X)) \\ &= \exp\left(-H_0(T)e^{\sum_{i=1}^{p} x_i\beta_i}\right) \\ &= \left[e^{-H_0(T)}\right]^{e^{\sum_{i=1}^{p} x_i\beta_i}} \\ &= S_0(T)^{e^{\sum_{i=1}^{p} x_i\beta_i}}\end{aligned}$$

Note that the survival time T is present in $S_0(T)$, but not in $e^{\sum_{i=1}^{p} x_i\beta_i}$.

A Note On Using e

The discussion that follows uses the terms exp(*x*) and e^x. These terms are identical. That is

$$\begin{aligned}\exp(x) &= e^x \\ &= (2.71828182846)^x\end{aligned}$$

The decision as to which form to use depends on the context. The preferred form is e^x. But often, the expression used for *x* becomes so small that it cannot be printed. In these situations, the exp(*x*) form will be used.

One other point needs to be made while we are on this subject. People often wonder why we use the number *e*. After all, *e* is an unfamiliar number that cannot be expressed exactly. Why not use a more common number like 2, 3, or 10? The answer is that it does matter because the choice of the base is arbitrary in that you can easily switch from one base to another. That is, it is easy to find constants *a*, *b*, and *c* so that

$$e = 2^a = 3^b = 10^c$$

In fact, *a* is 1/ln(2) = 1.4427, *b* is 1/ln(3)=0.9102, and *c* is 1/ln(10) = 0.4343. Using these constants, it is easy to switch from one base to another. For example, suppose a calculate only computes 10^x and we need the value of e^3. This can be computed as follows

$$\begin{aligned}e^3 &= \left(10^{0.4343}\right)^3 \\ &= 10^{3(0.4343)} \\ &= 10^{1.3029} \\ &= 20.0855\end{aligned}$$

The point is, it is simple to change from base *e* to base 3 to base 10. The number *e* is used for mathematical convenience.

Maximum Likelihood Estimation

Let $t = 1,\cdots,M$ index the *M* unique failure times $T_1, T_2, ..., T_M$. Note that *M* does not include duplicate times or censored observations. The set of all failures (deaths) that occur at time T_t is referred to as D_t. Let c and $d = 1,\cdots,m_t$ index the members of D_t. The set of all individuals that are at risk immediately before time T_t is referred to as R_t. This set, often called the *risk set*, includes all individuals that fail at time T_t as well as those that are censored or fail at a time later than T_t. Let $r = 1,\cdots,n_t$ index the members of R_t. Let *X* refer to a set of *p* covariates. These covariates are indexed by the subscripts *i*, *j*, or *k*. The values of the covariates at a particular failure time T_d are written $x_{1d}, x_{2d},\cdots,x_{pd}$ or x_{id} in general. The regression coefficients to be estimated are $\beta_1, \beta_2,\cdots,\beta_p$.

The Log Likelihood

When there are no ties among the failure times, the log likelihood is given by Kalbfleisch and Prentice (1980) as

$$\begin{aligned}LL(\beta) &= \sum_{t=1}^{M}\left\{\left(\sum_{i=1}^{p} x_{it}\beta_i\right) - \ln\left(\sum_{r\in R_t}\exp\left(\sum_{i=1}^{p} x_{ir}\beta_i\right)\right)\right\} \\ &= \sum_{t=1}^{M}\left\{\sum_{i=1}^{p} x_{it}\beta_i - \ln\left(G_{R_t}\right)\right\}\end{aligned}$$

where

$$G_R = \sum_{r \in R} \exp\left(\sum_{i=1}^{p} x_{ir} \beta_i \right)$$

The following notation for the first-order and second-order partial derivatives will be useful in the derivations in this section.

$$\begin{aligned} H_{jR} &= \frac{\partial G_R}{\partial \beta_j} \\ &= \sum_{r \in R} x_{jr} \exp\left(\sum_{i=1}^{p} x_{ir} \beta_i \right) \end{aligned}$$

$$\begin{aligned} A_{jkR} &= \frac{\partial^2 G_R}{\partial \beta_j \partial \beta_k} \\ &= \frac{\partial H_{jR}}{\partial \beta_k} \\ &= \sum_{r \in R} x_{jr} x_{kr} \exp\left(\sum_{i=1}^{p} x_{ir} \beta_i \right) \end{aligned}$$

The maximum likelihood solution is found by the Newton-Raphson method. This method requires the first and second order partial derivatives. The first order partial derivatives are

$$\begin{aligned} U_j &= \frac{\partial LL(\beta)}{\partial \beta_j} \\ &= \sum_{t=1}^{M} \left\{ x_{jt} - \frac{H_{jR_t}}{G_{R_t}} \right\} \end{aligned}$$

The second order partial derivatives, which are the information matrix, are

$$I_{jk} = \sum_{t=1}^{M} \frac{1}{G_{R_t}} \left(A_{jkR_t} - \frac{H_{jR_t} H_{kR_t}}{G_{R_t}} \right)$$

When there are failure time ties (note that censor ties are not a problem), the exact likelihood is very cumbersome. **NCSS** allows you to select either the approximation proposed by Breslow (1974) or the approximation given by Efron (1977). Breslow's approximation was used by the first Cox regression programs, but Efron's approximation provides results that are usually closer to the results given by the exact algorithm and it is now the preferred approximation (see for example Homer and Lemeshow (1999). We have included Breslow's method because of its popularity. For example, Breslow's method is the default method used in SAS.

Breslow's Approximation to the Log Likelihood

The log likelihood of Breslow's approximation is given by Kalbfleisch and Prentice (1980) as

$$\begin{aligned} LL(\beta) &= \sum_{t=1}^{M} \left\{ \left(\sum_{d \in D_t} \sum_{i=1}^{p} x_{id} \beta_i \right) - m_t \ln\left[\sum_{r \in R_t} \exp\left(\sum_{i=1}^{p} x_{ir} \beta_i \right) \right] \right\} \\ &= \sum_{t=1}^{M} \left\{ \sum_{d \in D_t} \sum_{i=1}^{p} x_{id} \beta_i - m_t \ln\left(G_{R_t} \right) \right\} \end{aligned}$$

where

$$G_R = \sum_{r \in R} \exp\left(\sum_{i=1}^{p} x_{ir} \beta_i \right)$$

The maximum likelihood solution is found by the Newton-Raphson method. This method requires the first-order and second-order partial derivatives. The first order partial derivatives are

$$\begin{aligned} U_j &= \frac{\partial LL(\beta)}{\partial \beta_j} \\ &= \sum_{t=1}^{M} \left\{ \left(\sum_{d \in D_t} x_{jd} \right) - \left(m_t \frac{H_{jR_t}}{G_{R_t}} \right) \right\} \end{aligned}$$

The negative of the second-order partial derivatives, which form the information matrix, are

$$I_{jk} = \sum_{t=1}^{M} \frac{m_t}{G_{R_t}} \left(A_{jkR_t} - \frac{H_{jR_t} H_{kR_t}}{G_{R_t}} \right)$$

Efron's Approximation to the Log Likelihood

The log likelihood of Efron's approximation is given by Kalbfleisch and Prentice (1980) as

$$\begin{aligned} LL(\beta) &= \sum_{t=1}^{M} \left\{ \sum_{d \in D_t} \sum_{i=1}^{p} x_{id} \beta_i - \sum_{d \in D_t} \ln \left[\sum_{r \in R_t} \exp\left(\sum_{i=1}^{p} x_{ir} \beta_i \right) - \frac{d-1}{m_t} \sum_{c \in D_t} \exp\left(\sum_{i=1}^{p} x_{ic} \beta_i \right) \right] \right\} \\ &= \sum_{t=1}^{M} \left\{ \sum_{d \in D_t} \sum_{i=1}^{p} x_{id} \beta_i - \sum_{d \in D_t} \ln \left[G_{R_t} - \frac{d-1}{m_t} G_{D_t} \right] \right\} \end{aligned}$$

The maximum likelihood solution is found by the Newton-Raphson method. This method requires the first and second order partial derivatives. The first partial derivatives are

$$\begin{aligned} U_j &= \frac{\partial LL(\beta)}{\partial \beta_j} \\ &= \sum_{t=1}^{M} \sum_{d \in D_t} \left(x_{jd} - \frac{H_{jR_t} - \left(\frac{d-1}{m_t} \right) H_{jD_t}}{G_{R_t} - \left(\frac{d-1}{m_t} \right) G_{D_t}} \right) \\ &= \sum_{t=1}^{M} \sum_{d \in D_t} x_{jd} - \sum_{t=1}^{M} \sum_{d=1}^{m_t} \left(\frac{H_{jR_t} - \left(\frac{d-1}{m_t} \right) H_{jD_t}}{G_{R_t} - \left(\frac{d-1}{m_t} \right) G_{D_t}} \right) \end{aligned}$$

The second partial derivatives provide the information matrix which estimates the covariance matrix of the estimated regression coefficients. The negative of the second partial derivatives are

$$I_{jk} = -\frac{\partial^2 LL(\beta)}{\partial\beta_j \partial\beta_k}$$
$$= \sum_{t=1}^{M}\sum_{d=1}^{m_t} \frac{\left(G_{R_t} - \left(\frac{d-1}{m_t}\right)G_{D_t}\right)\left(A_{jkR_t} - \left(\frac{d-1}{m_t}\right)A_{jkD_t}\right) - \left(H_{jR_t} - \left(\frac{d-1}{m_t}\right)H_{jD_t}\right)\left(H_{kR_t} - \left(\frac{d-1}{m_t}\right)H_{kD_t}\right)}{\left(G_{R_t} - \left(\frac{d-1}{m_t}\right)G_{D_t}\right)^2}$$

Estimation of the Survival Function

Once the maximum likelihood estimates have been obtained, it may be of interest to estimate the survival probability of a new or existing individual with specific covariate settings at a particular point in time. The methods proposed by Kalbfleisch and Prentice (1980) are used to estimate the survival probabilities.

Cumulative Survival

This estimates the cumulative survival of an individual with a set of covariates all equal to zero. The survival for an individual with covariate values of X_0 is

$$S(T \mid X_0) = \exp(H(T \mid X_0))$$
$$= \exp\left(H_0(T \mid X_0)\exp\sum_{i=1}^{p} x_{i0}\beta\right)$$
$$= [S_0(T)]^{\exp\sum_{i=1}^{p} x_{i0}\beta}$$

The estimate of the baseline survival function $S_0(T)$ is calculated from the cumulated hazard function using

$$S_0(T_0) = \prod_{T_t \le T_0} \alpha_t$$

where

$$\alpha_t = \frac{S(T_t)}{S(T_{t-1})}$$
$$= \left[\frac{S_0(T_t)}{S_0(T_{t-1})}\right]^{\exp\left(\sum_{i=1}^{p} x_{it}\beta_i\right)}$$
$$= \left[\frac{S_0(T_t)}{S_0(T_{t-1})}\right]^{\theta_t}$$

where

$$\theta_r = \exp\left(\sum_{i=1}^{p} x_{ir}\beta_i\right)$$

The value of α_t, the conditional baseline survival probability at time *T*, is the solution to the conditional likelihood equation

$$\sum_{d \in D_t} \frac{\theta_d}{1-\alpha_t^{\theta_d}} = \sum_{r \in R_t} \theta_r$$

When there are no ties at a particular time point, D_t contains one individual and the above equation can be solved directly, resulting in the solution

$$\hat{\alpha}_t = \left[1 - \frac{\hat{\theta}_t}{\sum_{r \in R_t} \hat{\theta}_r} \right]^{\hat{\theta}_t^{-1}}$$

When there are ties, the equation must be solved iteratively. The starting value of this iterative process is

$$\hat{\alpha}_t = \exp\left(\frac{-m_t}{\sum_{r \in R_t} \hat{\theta}_r} \right)$$

Baseline Hazard Rate

Hosmer and Lemeshow (1999) estimate the baseline hazard rate $h_0(T_t)$ as follows

$$h_0(T_t) = 1 - \alpha_t$$

They mention that this estimator will typically be too unstable to be of much use. To overcome this, you might smooth these quantities using lowess function of the Scatter Plot program.

Cumulative Hazard

An estimate of the cumulative hazard function $H_0(T)$ derived from relationship between the cumulative hazard and the cumulative survival. The estimated baseline survival is

$$\hat{H}_0(T) = -\ln\left(\hat{S}_0(T)\right)$$

This leads to the estimated cumulative hazard function is

$$\hat{H}(T) = -\exp\left(\sum_{i=1}^{p} x_i \hat{\beta}_i \right) \ln\left(\hat{S}_0(T)\right)$$

Cumulative Survival

The estimate of the cumulative survival of an individual with a set of covariates values of X_0 is

$$\hat{S}(T \mid X_0) = \hat{S}_0(T)^{\exp \sum_{i=1}^{p} x_{i0} \hat{\beta}_i}$$

Statistical Tests and Confidence Intervals

Inferences about one or more regression coefficients are all of interest. These inference procedures can be treated by considering hypothesis tests and/or confidence intervals. The inference procedures in Cox regression rely on large sample sizes for accuracy.

Two tests are available for testing the significance of one or more independent variables in a regression: the likelihood ratio test and the Wald test. Simulation studies usually show that the likelihood ratio test performs better than the Wald test. However, the Wald test is still used to test the significance of individual regression coefficients because of its ease of calculation.

These two testing procedures will be described next.

Likelihood Ratio and Deviance

The *Likelihood Ratio* test statistic is -2 times the difference between the log likelihoods of two models, one of which is a subset of the other. The distribution of the LR statistic is closely approximated by the chi-square distribution for large sample sizes. The degrees of freedom (DF) of the approximating chi-square distribution is equal to the difference in the number of regression coefficients in the two models. The test is named as a ratio rather than a difference since the difference between two log likelihoods is equal to the log of the ratio of the two likelihoods. That is, if L_{full} is the log likelihood of the full model and L_{subset} is the log likelihood of a subset of the full model, the likelihood ratio is defined as

$$\begin{aligned} LR &= -2\left[L_{\text{subset}} - L_{\text{full}}\right] \\ &= -2\left[\ln\left(\frac{l_{\text{subset}}}{l_{\text{full}}}\right)\right] \end{aligned}$$

Note that the -2 adjusts *LR* so the chi-square distribution can be used to approximate its distribution.

The likelihood ratio test is the test of choice in Cox regression. Various simulation studies have shown that it is more accurate than the Wald test in situations with small to moderate sample sizes. In large samples, it performs about the same. Unfortunately, the likelihood ratio test requires more calculations than the Wald test, since it requires the fitting of two maximum-likelihood models.

Deviance

When the full model in the likelihood ratio test statistic is the saturated model, *LR* is referred to as the *deviance*. A saturated model is one which includes all possible terms (including interactions) so that the predicted values from the model equal the original data. The formula for the deviance is

$$D = -2\left[L_{\text{Reduced}} - L_{\text{Saturated}}\right]$$

The deviance in Cox regression is analogous to the residual sum of squares in multiple regression. In fact, when the deviance is calculated in multiple regression, it is equal to the sum of the squared residuals.

The change in deviance, ΔD, due to excluding (or including) one or more variables is used in Cox regression just as the partial *F* test is used in multiple regression. Many texts use the letter *G* to represent ΔD. Instead of using the *F* distribution, the distribution of the change in deviance is approximated by the chi-square distribution. Note that since the log likelihood for the saturated model is common to both deviance values, ΔD can be calculated without actually fitting the saturated model. This fact becomes very important during subset selection. The formula for ΔD for testing the significance of the regression coefficient(s) associated with the independent variable *X*1 is

$$\begin{aligned} \Delta D_{X1} &= D_{\text{without } X1} - D_{\text{with } X1} \\ &= -2\left[L_{\text{without } X1} - L_{\text{Saturated}}\right] + 2\left[L_{\text{with } X1} - L_{\text{Saturated}}\right] \\ &= -2\left[L_{\text{without } X1} - L_{\text{with } X1}\right] \end{aligned}$$

Note that this formula looks identical to the likelihood ratio statistic. Because of the similarity between the change in deviance test and the likelihood ratio test, their names are often used interchangeably.

Wald Test

The Wald test will be familiar to those who use multiple regression. In multiple regression, the common *t*-test for testing the significance of a particular regression coefficient is a Wald test. In Cox regression, the Wald test is calculated in the same manner. The formula for the Wald statistic is

$$z_j = \frac{b_j}{s_{b_j}}$$

where s_{b_j} is an estimate of the standard error of b_j provided by the square root of the corresponding diagonal element of the covariance matrix, $V\left(\hat{\beta}\right) = I^{-1}$.

With large sample sizes, the distribution of z_j is closely approximated by the normal distribution. With small and moderate sample sizes, the normal approximation is described as "adequate."

The Wald test is used in **NCSS** to test the statistical significance of individual regression coefficients.

Confidence Intervals

Confidence intervals for the regression coefficients are based on the Wald statistics. The formula for the limits of a $100(1-\alpha)\%$ two-sided confidence interval is

$$b_j \pm |z_{\alpha/2}| s_{b_j}$$

R^2

Hosmer and Lemeshow (1999) indicate that at the time of the writing of their book, there is no single, easy to interpret measure in Cox regression that is analogous to R^2 in multiple regression. They indicate that if such a measure "must be calculated" they would use

$$R_p^2 = 1 - \exp\left[\frac{2}{n}\left(L_0 - L_p\right)\right]$$

where L_0 is the log likelihood of the model with no covariates, *n* is the number of observations (censored or not), and L_p is the log likelihood of the model that includes the covariates.

Subset Selection

Subset selection refers to the task of finding a small subset of the available regressor variables that does a good job of predicting the dependent variable. Because Cox regression must be solved iteratively, the task of finding the best subset can be time consuming. Hence, techniques which look at all possible combinations of the regressor variables are not feasible. Instead, algorithms that add or remove a variable at each step must be used. Two such searching algorithms are available in this module: forward selection and forward selection with switching.

Before discussing the details of these two algorithms, it is important to comment on a couple of issues that can come up. The first issue is what to do about the binary variables that are generated for a categorical independent variable. If such a variable has six categories, five binary variables are generated. You can see that with two or three categorical variables, a large number of binary variables may result, which greatly increases the total number of variables that must be searched. To avoid this problem, the algorithms used here search on model terms rather than on the individual variables. Thus, the whole set of binary variables associated with a given term are considered together for inclusion in, or deletion from, the model. It's all or none. Because of the time

consuming nature of the algorithm, this is the only feasible way to deal with categorical variables. If you want the subset algorithm to deal with them individually, you can generate the set of binary variables manually and designate them as Numeric Variables.

Hierarchical Models

A second issue is what to do with interactions. Usually, an interaction is not entered in the model unless the individual terms that make up that interaction are also in the model. For example, the interaction term A*B*C is not included unless the terms A, B, C, A*B, A*C, and B*C are already in the model. Such models are said to be *hierarchical*. You have the option during the search to force the algorithm to only consider hierarchical models during its search. Thus, if C is not in the model, interactions involving C are not even considered. Even though the option for non-hierarchical models is available, we recommend that you only consider hierarchical models.

Forward Selection

The method of forward selection proceeds as follows.

1. Begin with no terms in the model.
2. Find the term that, when added to the model, achieves the largest value of *R*-squared. Enter this term into the model.
3. Continue adding terms until a preset limit on the maximum number of terms in the model is reached.

This method is comparatively fast, but it does not guarantee that the best model is found except for the first step when it finds the best single term. You might use it when you have a large number of observations so that other, more time consuming methods, are not feasible, or when you have far too many possible regressor variables and you want to reduce the number of terms in the selection pool.

Forward Selection with Switching

This method is similar to the method of Forward Selection discussed above. However, at each step when a term is added, all terms in the model are switched one at a time with all candidate terms not in the model to determine if they increase the value of *R*-squared. If a switch can be found, it is made and the candidate terms are again searched to determine if another switch can be made.

When the search for possible switches does not yield a candidate, the subset size is increased by one and a new search is begun. The algorithm is terminated when a target subset size is reached or all terms are included in the model.

Discussion

These algorithms usually require two runs. In the first run, you set the maximum subset size to a large value such as 10. By studying the Subset Selection reports from this run, you can quickly determine the optimum number of terms. You reset the maximum subset size to this number and make the second run. This two-step procedure works better than relying on some F-to-enter and F-to-remove tests whose properties are not well understood to begin with.

Residuals

The following presentation summarizes the discussion on residuals found in Klein and Moeschberger (1997) and Hosmer and Lemeshow (1999). For a more thorough treatment of this topic, we refer you to either of these books.

In most settings in which residuals are studied, the dependent variable is predicted using a model based on the independent variables. In these cases, the residual is simply the difference between the actual value and the predicted value of the dependent variable. Unfortunately, in Cox regression there is no obvious analog this actual minus predicted. Realizing this, statisticians have looked at how residuals are used and then, based on those uses,

developed quantities that meet those needs. They call these quantities *residuals* because they are used in place of residuals. However, you must remember that they are not equivalent to usual the residuals that you see in multiple regression, for example.

In the discussion that follows, the formulas will be simplified if we use the substitution

$$\theta_r = \exp\left(\sum_{i=1}^{p} x_{ir}\beta_i\right)$$

Cox-Snell Residuals

The Cox-Snell residuals were used to assess the goodness-of-fit of the Cox regression. The Cox-Snell residuals are defined as

$$r_t = H_{B0}(T_t)\theta_t$$

where the *b*'s are the estimated regression coefficients and $H_0(T_t)$ is Breslow's estimate of the cumulative baseline hazard function. This value is defined as follows

$$H_{B0}(T_t) = \sum_{T_i \le T_t}\left[\frac{m_i}{\sum_{j \in R_{T_i}}\theta_j}\right]$$

The Cox-Snell residuals were the first to be proposed in the literature. They have since been replaced by other types of residuals and are now only of historical interest. See, for example, the discussion of Marubini and Valsecchi (1996) who state that the use of these residuals on distributional grounds should be avoided.

Martingale Residuals

Martingale residuals cannot be used to assess goodness-of-fit as are the usual residuals in multiple regression. The best model need not have the smallest sum of squared martingale residuals. Martingale residuals follow the unit exponential distribution. Some authors suggested analyzing these residuals to determine how close they are to the exponential distribution, hoping that a lack of exponentiality indicated a lack of fit. Unfortunately, just the opposite is the case since in a model with no useful covariates, these residuals are exactly exponential in distribution. Another diagnostic tool for in regular multiple regression is a plot of the residuals versus the fitted values. Here again, the martingale residuals cannot be used for this purpose since they are negatively correlated with the fitted values.

So of what use are martingale residuals? They have two main uses. First, they can be used to find outliers—individuals who are poorly fit by the model. Second, martingale residuals can be used to determine the functional form of each of the covariates in the model.

Finding Outliers

The martingale residuals are defined as

$$M_t = c_t - r_t$$

where c_t is one if there is a failure at time T_t and zero otherwise. The martingale residual measures the difference between whether an individual experiences the event of interest and the expected number of events based on the model. The maximum value of the residual is one and the minimum possible value is negative infinity. Thus, the residual is highly skewed. A large negative martingale residual indicates a high risk individual who still had a long survival time.

Finding the Function Form of Covariates

Martingale residuals can be used to determine the functional form of a covariate. To do this, you generate the Martingale residuals from a model without the covariates. Next, you plot these residuals against the value of the covariate. For large datasets, this may be a time consuming process. Therneau and Grambsch (2000) suggest that the martingale residuals from a model with no covariates be plotted against each of the covariates. These plots will reveal the appropriate functional form of the covariates in the model so long as the covariates are not highly correlated among themselves.

Deviance Residuals

Deviance residuals are used to search for outliers. The deviance residuals are defined as

$$DEV_t = sign(M_t)\sqrt{-2[M_t + c_t \ln(c_t - M_t)]}$$

or zero when M_t is zero. These residuals are plotted against the risk scores given by

$$\exp\left(\sum_{i=1}^{p} x_{it} b_i\right)$$

When there is slight to moderate censoring, large absolute values in these residuals point to potential outliers. When there is heavy censoring, there will be a large number of residuals near zero. However, large absolute values will still indicate outliers.

Schoenfeld's Residuals

A set of *p* Schoenfeld residuals is defined for each noncensored individual. The residual is missing when the individual is censored. The Schoenfeld residuals are defined as follows

$$\begin{aligned} r_{it} &= c_t\left[x_{it} - \frac{\sum_{r\in R_t} x_{ir}\theta_r}{\sum_{r\in R_t}\theta_r}\right] \\ &= c_t\left[x_{it} - \sum_{r\in R_t} x_{ir} w_r\right] \end{aligned}$$

where

$$w_r = \frac{\sum_{r\in R_t} x_{ir}\theta_r}{\sum_{r\in R_t}\theta_r}$$

Thus this residual is the difference between the actual value of the covariate and a weighted average where the weights are determined from the risk scores.

These residuals are used to estimate the influence of an observation on each of the regression coefficients. Plots of these quantities against the row number or against the corresponding covariate values are used to study these residuals.

Scaled Schoenfeld's Residuals

Hosmer and Lemeshow (1999) and Therneau and Grambsch (2000) suggest that scaling the Schoenfeld residuals by an estimate of their variance gives quantities with greater diagnostic ability. Hosmer and Lemeshow (1999) use the covariance matrix of the regression coefficients to perform the scaling. The scaled Schoenfeld residuals are defined as follows

$$r_{kt}^* = m\sum_{i=1}^{p} V_{ik} r_{it}$$

where m is the total number of deaths in the dataset and V is the estimated covariance matrix of the regression coefficients.

These residuals are plotted against time to validate the proportional hazards assumption. If the proportional hazards assumption holds, the residuals will fall randomly around a horizontal line centered at zero. If the proportional hazards assumption does not hold, a trend will be apparent in the plot.

Data Structure

Survival data sets require up to three components for the survival time: the ending survival time, the beginning survival time during which the subject was not observed, and an indicator of whether the observation was censored or failed.

Based on these three components, various types of data may be analyzed. *Right censored* data are specified using only the ending time variable and the censor variable. *Left truncated* and *Interval* data are entered using all three variables.

The table below shows survival data ready for analysis. These data are from a lung cancer study reported in Kalbfleisch (1980), page 223. These data are in the LungCancer dataset. The variables are

TIME	days of survival
CENSOR	censor indicator
STATUS	performance status
MONTHS	months from diagnosis
AGE	age in years
THERAPY	prior therapy

LungCancer dataset (subset)

TIME	CENSOR	STATUS	MONTHS	AGE	THERAPY
72	1	60	7	69	0
411	1	70	5	64	10
228	1	60	3	38	0
126	1	60	9	63	10
118	1	70	11	65	10
10	1	20	5	49	0
82	1	40	10	69	10
110	1	80	29	68	0
314	1	50	18	43	0
100	0	70	6	70	0
42	1	60	4	81	0
8	1	40	58	63	10
144	1	30	4	63	0
25	0	80	9	52	10
11	1	70	11	48	10

Procedure Options

This section describes the options available in this procedure.

Variables, Model Tab

This panel lets you designate which variables and model are used in the analysis.

Variables

Time Variable

This variable contains the length of time that an individual was observed. This may represent a failure time or a censor time. Whether the subject actually died is specified by the Censor variable. Since the values are elapsed times, they must be positive. Zeroes and negative values are treated as missing values.

During the maximum likelihood calculations, a risk set is defined for each individual. The risk set is defined to be those subjects who were being observed at this subject's failure and who lived as long or longer. It may take several rows of data to specify a subject's history.

This variable and the Entry Time variable define a period during which the individual was at risk of failing. If the Entry Time is not specified, its value is assumed to be zero.

Several types of data may be entered. These will be explained next.

- **Failure**

  This type of data occurs when a subject is followed from their entrance into the study until their death. The failure time is entered in this variable and the Censor variable is set to the failed code, which is often a one.

  The Entry Time Variable is not necessary. If an Entry Time variable is used, its value should be zero for this type of observation.

- **Interval Failure**

  This type of data occurs when a subject is known to have died during a certain interval. The subject may, or may not, have been observed during other intervals. If they were, they are treated as Interval Censored data. An individual may require several rows on the database to record their complete follow-up history.

  For example, suppose the condition of the subjects is only available at the end of each month. If a subject fails during the fifth month, two rows of data would be required. One row, representing the failure, would have a Time of 5.0 and an Entry Time of 4.0. The Censor variable would contain the failure code. A second row, representing the prior periods, would have a Time of 4.0 and an Entry Time of 0.0. The Censor variable would contain the censor code.

- **Censored**

  This type of data occurs when a subject has not failed up to the specified time. For example, suppose that a subject enters the study and does not die until after the study ends 12 months later. The subject's time (365 days) is entered here. The Censor variable contains the censor code.

- **Interval Censored**

  This type of data occurs when a subject is known not to have died during a certain interval. The subject may, or may not, have been observed during other intervals. An individual may require several rows on the database to record their complete follow-up history.

For example, suppose the condition of the subjects is only available at the end of each month. If a subject fails during the fifth month, two rows of data would be required. One row, representing the failure, would have a Time of 5.0 and an Entry Time of 4.0. The Censor variable would contain the failure code. A second row, representing the prior periods, would have a Time of 4.0 and an Entry Time of 0.0. The Censor variable would contain the censor code.

Ties Method

The basic Cox regression model assumes that all failure times are unique. When ties exist among the failure times, one of two approximation methods is used to deal with the ties. When no ties are present, both of these methods result in the same estimates.

- **Breslow**

  This method was suggested first and is the default in many programs. However, the Efron method has been shown to be more accurate in most cases. The Breslow method is only used when you want to match the results of some other (older) Cox regression package.

- **Efron**

  This method has been shown to be more accurate, but requires slightly more time to calculate. This is the recommended method.

Entry Time Variable

This optional variable contains the elapsed time before an individual entered the study. Usually, this value is zero. However, in cases such as *left truncation* and *interval censoring*, this value defines a time period before which the individual was not observed.

Negative entry times are treated as missing values. It is possible for the entry time to be zero.

Censor Variable

The values in this variable indicate whether the value of the Time Variable represents a censored time or a failure time. These values may be text or numeric. The interpretation of these codes is specified by the Failed and Censored options to the right of this option.

Only two values are used, the Failure code and the Censor code. The Unknown Type option specifies what is to be done with values that do not match either the Failure code or the Censor code.

Rows with missing values (blanks) in this variable are omitted from the estimation phase, but results are shown in any reports that output predicted values.

Failure

This value identifies those values of the Censor Variable that indicate that the Time Variable gives a failure time. The value may be a number or a letter.

We suggest the letter ‘F’ or the number ‘1’ when you are in doubt as to what to use.

A failed observation is one in which the time until the event of interest was measured exactly; for example, the subject died of the disease being studied. The exact failure time is known.

Left Censoring

When the exact failure time is not known, but instead only an upper bound on the failure time is known, the time value is said to have been *left censored*. In this case, the time value is treated as if it were the true failure time, not just an upper bound. So left censored observations should be coded as failed observations.

Censor

This value identifies those values of the Censor Variable that indicate that the individual recorded on this row was censored. That is, the actual failure time occurs sometime after the value of the Time Variable.

We suggest the letter 'C' or the number '0' when you are in doubt as to what to use.

A censored observation is one in which the time until the event of interest is not known because the individual withdrew from the study, the study ended before the individual failed, or for some similar reason.

Note that it does not matter whether the censoring was Right or Interval. All you need to indicate here is that they were censored.

Other Censor

This option specifies what the program is to assume about observations whose censor value is not equal to either the *Failure* code or the *Censor* code. Note that observations with missing censor values are always treated as missing.

- **Censored**
  Observations with unknown censor values are assumed to have been censored.

- **Failed**
  Observations with unknown censor values are assumed to have failed.

- **Missing**
  Observations with unknown censor values are assumed to be missing and they are removed from the analysis.

Numeric X's

Specify the numeric (continuous) independent variables. By numeric, we mean that the values are numeric and at least ordinal. Nominal variables, even when coded with numbers, should be specified as Categorical Independent Variables. Although you may specify binary (0-1) variables here, they are better analyzed when you specify them as Categorical Independent Variables.

If you want to create powers and cross-products of these variables, specify an appropriate model in the 'Custom Model' field under the Model tab.

If you want to create hazard values for values of X not in your database, add the X values to the bottom of the database and leave their time and censoring blank. They will not be used during estimation, but various hazard and survival statistics will be generated for them and displayed in the Predicted Values report.

Categorical X's

Specify categorical (nominal or group) independent variables in this box. By categorical we mean that the variable has only a few unique, numeric or text, values like 1, 2, 3 or Yes, No, Maybe. The values are used to identify categories.

Regression analysis is only defined for numeric variables. Since categorical variables are nominal, they cannot be used directly in regression. Instead, an internal set of numeric variables must be substituted for each categorical variable.

Suppose a categorical variable has G categories. **NCSS** automatically generates the G-1 internal, numeric variables for the analysis. The way these internal variables are created is determined by the Recoding Scheme and, if needed, the Reference Value. These options can be entered separately with each categorical variable, or they can specified using a default value (see Default Recoding Scheme and Default Reference Value below).

The syntax for specifying a categorical variable is *VarName*(*CType; RefValue*) where *VarName* is the name of the variable, CType is the recoding scheme, and RefValue is the reference value, if needed.

CType

The recoding scheme is entered as a letter. Possible choices are B, P, R, N, S, L, F, A, 1, 2, 3, 4, 5, or E. The meaning of each of these letters is as follows.

- **B** for **binary** (the group with the reference value is skipped).
  Example: Categorical variable Z with 4 categories. Category D is the reference value.

Z	B1	B2	B3
A	1	0	0
B	0	1	0
C	0	0	1
D	0	0	0

- **P** for **Polynomial** of up to 5th order (you cannot use this option with category variables with more than 6 categories.
  Example: Categorical variable Z with 4 categories.

Z	P1	P2	P3
1	-3	1	-1
3	-1	-1	3
5	1	-1	-3
7	3	1	1

- **R** to compare each with the **reference value** (the group with the reference value is skipped).
  Example: Categorical variable Z with 4 categories. Category D is the reference value.

Z	C1	C2	C3
A	1	0	0
B	0	1	0
C	0	0	1
D	-1	-1	-1

- **N** to compare each with the **next** category.
  Example: Categorical variable Z with 4 categories.

Z	S1	S2	S3
1	1	0	0
3	-1	1	0
5	0	-1	1
7	0	0	-1

- **S** to compare each with the **average of all subsequent** values.
  Example: Categorical variable Z with 4 categories.

Z	S1	S2	S3
1	-3	0	0
3	1	-2	0
5	1	1	-1
7	1	1	1

- **L** to compare each with the **prior** category.
  Example: Categorical variable Z with 4 categories.

Z	S1	S2	S3
1	-1	0	0
3	1	-1	0
5	0	1	-1
7	0	0	1

- **F** to compare each with the **average of all prior** categories.
  Example: Categorical variable Z with 4 categories.

Z	S1	S2	S3
1	1	1	1
3	1	1	-1
5	1	-2	0
7	-3	0	0

- **A** to compare each with the **average of all** categories (the Reference Value is skipped).
  Example: Categorical variable Z with 4 categories. Suppose the reference value is 3.

Z	S1	S2	S3
1	-3	1	1
3	1	1	1
5	1	-3	1
7	1	1	-3

- **1** to compare each with the **first** category after sorting.
  Example: Categorical variable Z with 4 categories.

Z	C1	C2	C3
A	-1	-1	-1
B	1	0	0
C	0	1	0
D	0	0	1

- **2** to compare each with the **second** category after sorting.
  Example: Categorical variable Z with 4 categories.

Z	C1	C2	C3
A	1	0	0
B	-1	-1	-1
C	0	1	0
D	0	0	1

- **3** to compare each with the **third** category after sorting.
  Example: Categorical variable Z with 4 categories.

Z	C1	C2	C3
A	1	0	0
B	0	1	0
C	-1	-1	-1
D	0	0	1

- **4** to compare each with the **fourth** category after sorting.
  Example: Categorical variable Z with 4 categories.

Z	C1	C2	C3
A	1	0	0
B	0	1	0
C	0	0	1
D	-1	-1	-1

- **5** to compare each with the **fifth** category after sorting.
  Example: Categorical variable Z with 5 categories.

Z	C1	C2	C3	C4
A	1	0	0	0
B	0	1	0	0
C	0	0	1	0
D	0	0	0	1
E	-1	-1	-1	-1

- **E** to compare each with the **last** category after sorting.
  Example: Categorical variable Z with 4 categories.

Z	C1	C2	C3
A	1	0	0
B	0	1	0
C	0	0	1
D	-1	-1	-1

RefValue
A second, optional argument is the reference value. The reference value is one of the categories. The other categories are compared to it, so it is usually a baseline or control value. If neither a baseline or control value is evident, the reference value is the most frequent value.

For example, suppose you want to include a categorical independent variable, State, which has four values: Texas, California, Florida, and NewYork. Suppose the recoding scheme is specified as *Compare Each with Reference Value* with the reference value of *California*. You would enter

State(R;California)

Default Recoding Scheme

Select the default type of numeric variable that will be generated when processing categorical independent variables. The values in a categorical variable are not used directly in regression analysis. Instead, a set of numeric variables is automatically created and substituted for them. This option allows you to specify what type of numeric variable will be created. The options are outlined in the sections below.

The contrast type may also be designated within parentheses after the name of each categorical independent variable, in which case the default contrast type is ignored.

If your model includes interactions of categorical variables, this option should be set to '*Contrast with Reference*' or *Compare with All Subsequent*' in order to match GLM results for factor effects.

- **Binary** (the group with the reference value is skipped).
  Example: Categorical variable Z with 4 categories. Category D is the reference value.

Z	B1	B2	B3
A	1	0	0
B	0	1	0
C	0	0	1
D	0	0	0

- **Polynomial** of up to 5th order (you cannot use this option with category variables with more than 6 categories.
  Example: Categorical variable Z with 4 categories.

Z	P1	P2	P3
1	-3	1	-1
3	-1	-1	3
5	1	-1	-3
7	3	1	1

- **Compare Each with Reference Value** (the group with the reference value is skipped).
  Example: Categorical variable Z with 4 categories. Category D is the reference value.

Z	C1	C2	C3
A	1	0	0
B	0	1	0
C	0	0	1
D	-1	-1	-1

- **Compare Each with Next**.
  Example: Categorical variable Z with 4 categories.

Z	S1	S2	S3
1	1	0	0
3	-1	1	0
5	0	-1	1
7	0	0	-1

- **Compare Each with All Subsequent**.
  Example: Categorical variable Z with 4 categories.

Z	S1	S2	S3
1	-3	0	0
3	1	-2	0
5	1	1	-1
7	1	1	1

- **Compare Each with Prior**
  Example: Categorical variable Z with 4 categories.

Z	S1	S2	S3
1	-1	0	0
3	1	-1	0
5	0	1	-1
7	0	0	1

- **Compare Each with All Prior**
  Example: Categorical variable Z with 4 categories.

Z	S1	S2	S3
1	1	1	1
3	1	1	-1
5	1	-2	0
7	-3	0	0

- **Compare Each with Average**
  Example: Categorical variable Z with 4 categories. Suppose the reference value is 3.

Z	S1	S2	S3
1	-3	1	1
3	1	1	1
5	1	-3	1
7	1	1	-3

- **Compare Each with First**
  Example: Categorical variable Z with 4 categories.

Z	C1	C2	C3
A	-1	-1	-1
B	1	0	0
C	0	1	0
D	0	0	1

- **Compare Each with Second**
  Example: Categorical variable Z with 4 categories.

Z	C1	C2	C3
A	1	0	0
B	-1	-1	-1
C	0	1	0
D	0	0	1

- **Compare Each with Third**
  Example: Categorical variable Z with 4 categories.

Z	C1	C2	C3
A	1	0	0
B	0	1	0
C	-1	-1	-1
D	0	0	1

- **Compare Each with Fourth**
  Example: Categorical variable Z with 4 categories.

Z	C1	C2	C3
A	1	0	0
B	0	1	0
C	0	0	1
D	-1	-1	-1

- **Compare Each with Fifth**
  Example: Categorical variable Z with 5 categories.

Z	C1	C2	C3	C4
A	1	0	0	0
B	0	1	0	0
C	0	0	1	0
D	0	0	0	1
E	-1	-1	-1	-1

- **Compare Each with Last**
  Example: Categorical variable Z with 4 categories.

Z	C1	C2	C3
A	1	0	0
B	0	1	0
C	0	0	1
D	-1	-1	-1

Default Reference Value

This option specifies the default reference value to be used when automatically generating indicator variables during the processing of selected categorical independent variables. The reference value is often the baseline, and the other values are compared to it. The choices are

- **First Value after Sorting – Fifth Value after Sorting**
  Use the first (through fifth) value in alpha-numeric sorted order as the reference value.

- **Last Value after Sorting**
  Use the last value in alpha-numeric sorted order as the reference value.

Frequencies

This is an optional variable containing the frequency (observation count) for each row. Usually, you would leave this option blank and let each row receive the default frequency of one.

If your data have already been summarized, this option lets you specify how many actual rows each physical row represents.

Regression Model

Terms

This option specifies which terms (terms, powers, cross-products, and interactions) are included in the regression model. For a straight-forward regression model, select *1-Way*.

The options are

- **1-Way**
  This option generates a model in which each variable is represented by a single model term. No cross-products, interactions, or powers are added. Use this option when you want to use the variables you have specified, but you do not want to generate other terms.

  This is the option to select when you want to analyze the independent variables specified without adding any other terms.

  For example, if you have three independent variables A, B, and C, this would generate the model:

  A + B + C

- **Up to 2-Way**
  This option specifies that all individual variables, two-way interactions, and squares of numeric variables are included in the model. For example, if you have three numeric variables A, B, and C, this would generate the model:

  A + B + C + A*B + A*C + B*C + A*A + B*B + C*C

  On the other hand, if you have three categorical variables A, B, and C, this would generate the model:

  A + B + C + A*B + A*C + B*C

- **Up to 3-Way**
  All individual variables, two-way interactions, three-way interactions, squares of numeric variables, and cubes of numeric variables are included in the model. For example, if you have three numeric, independent variables A, B, and C, this would generate the model:

  A + B + C + A*B + A*C + B*C + A*B*C + A*A + B*B + C*C + A*A*B + A*A*C + B*B*C +A*C*C + B*C*C

On the other hand, if you have three categorical variables A, B, and C, this would generate the model:

A + B + C + A*B + A*C + B*C + A*B*C

- **Up to 4-Way**
  All individual variables, two-way interactions, three-way interactions, and four-way interactions are included in the model. Also included would be squares, cubes, and quartics of numeric variables and their cross-products.

  For example, if you have four categorical variables A, B, C, and D, this would generate the model:

  A + B + C + D + A*B + A*C + A*D + B*C + B*D + C*D + A*B*C + A*B*D + A*C*D + B*C*D + A*B*C*D

- **Interaction**
  Mainly used for categorical variables. A saturated model (all terms and their interactions) is generated. This requires a dataset with no missing categorical-variable combinations (you can have unequal numbers of observations for each combination of the categorical variables). No squares, cubes, etc. are generated.

  For example, if you have three independent variables A, B, and C, this would generate the model:

  A + B + C + A*B + A*C + B*C + A*B*C

  Note that the discussion of the Custom Model option discusses the interpretation of this model.

- **Custom Model**
  The model specified in the *Custom Model* box is used.

Center X's

The values of the independent variables may be centered to improve the stability of the algorithm. An value is 'centered' when its mean is subtracted from it.

Centering does not change the values of the regression coefficients, except that the algorithm might provide slightly different results because of better numerical stability.

Centering does affect the values of the row-wise statistics such as XB, Exp(XB), S0, H0, and so on because it changes the value of X in these expressions. When the data are centered, the deviation from the mean (X-Xbar) is substituted for X in these expressions.

The options are available:

- **Unchecked**
  The data are not centered.

- **Checked**
  All variables, both numeric and binary, are centered.

Replace Custom Model with Preview Model (button)

When this button is pressed, the Custom Model is cleared and a copy of the Preview model is stored in the Custom Model. You can then edit this Custom Model as desired.

Maximum Order of Custom Terms

This option specifies that maximum number of variables that can occur in an interaction (or cross-product) term in a custom model. For example, A*B*C is a third order interaction term and if this option were set to 2, the A*B*C term would not be included in the model.

This option is particularly useful when used with the bar notation of a custom model to allow a simple way to remove unwanted high-order interactions.

Custom Model

This options specifies a custom model. It is only used when the *Terms* option is set to *Custom*. A custom model specifies the terms (single variables and interactions) that are to be kept in the model.

Interactions

An interaction expresses the combined relationship between two or more variables and the dependent variable by creating a new variable that is the product of the variables. The interaction between two numeric variables is generated by multiplying them. The interaction between to categorical variables is generated by multiplying each pair of indicator variables. The interaction between a numeric variable and a categorical variable is created by generating all products between the numeric variable and the indicator variables generated from the categorical variable.

Syntax

A model is written by listing one or more terms. The terms are separated by a blank or plus sign. Terms include variables and interactions. Specify regular variables (main effects) by entering the variable names. Specify interactions by listing each variable in the interaction separated by an asterisk (*), such as Fruit*Nuts or A*B*C.

You can use the bar (|) symbol as a shorthand technique for specifying many interactions quickly. When several variables are separated by bars, all of their interactions are generated. For example, A|B|C is interpreted as A + B + C + A*B + A*C + B*C + A*B*C.

You can use parentheses. For example, A*(B+C) is interpreted as A*B + A*C.

Some examples will help to indicate how the model syntax works:

A|B = A + B + A*B

A|B A*A B*B = A + B + A*B + A*A + B*B

Note that you should only repeat numeric variable. That is, A*A is valid for a numeric variable, but not for a categorical variable.

A|A|B|B (Max Term Order=2) = A + B + A*A + A*B + B*B

A|B|C = A + B + C + A*B + A*C + B*C + A*B*C

(A + B)*(C + D) = A*C + A*D + B*C + B*D

(A + B)|C = (A + B) + C + (A + B)*C = A + B + C + A*C + B*C

Subset Selection

Search Method

This option specifies the subset selection algorithm used to reduce the number of independent variables that used in the regression model. Note that since the solution algorithm is iterative, the selection process can be very time consuming. The Forward algorithm is much quicker than the Forward with Switching algorithm, but the Forward algorithm does not usually find as good of a model.

Also note that in the case of categorical independent variables, the algorithm searches among the original categorical variables, not among the generated individual binary variables. That is, either all binary variables associated with a particular categorical variable are included or not—they are not considered individually.

Hierarchical models are such that if an interaction is in the model, so are the terms that can be derived from it. For example, if A*B*C is in the model, so are A, B, C, A*B, A*C, and B*C. Statisticians usually adopt hierarchical models rather than non-hierarchical models. The subset selection procedure can be made to consider only hierarchical models during its search.

The subset selection options are:

- **None – No Search is Conducted**

  No subset selection is attempted. All specified independent variables are used in the regression equation.

- **(Hierarchical) Forward**

  With this algorithm, the term with the largest log likelihood is entered into the model. Next, the term that increases the log likelihood the most is added. This selection is continued until all the terms have been entered or until the maximum subset size has been reach.

  If hierarchical models are selected, only those terms that will keep the model hierarchical are candidates for selection. For example, the interaction term A*B will not be considered unless both A and B are already in the model.

  When using this algorithm, you must make one run that allows a large number of terms to find the appropriate number of terms. Next, a second run is made in which you decrease the maximum terms in the subset to the number after which the log likelihood does not change significantly.

- **(Hierarchical) Forward with Switching**

  This algorithm is similar to the Forward algorithm described above. The term with the largest log likelihood is entered into the regression model. The term which increases the log likelihood the most when combined with the first term is entered next. Now, each term in the current model is removed and the rest of the terms are checked to determine if, when they are used instead, the likelihood function is increased. If a term can be found by this switching process, the switch is made and the whole switching operation is begun again. The algorithm continues until no term can be found that improves the likelihood. This model then becomes the best two-term model.

  Next, the subset size is increased by one, the best third term is entered into the model, and the switching process is repeated. This process is repeated until the maximum subset size is reached. Hence, this model finds the optimum subset for each subset size. You must make one run to find an appropriate subset size by looking at the change in the log likelihood. You then reset the maximum subset size to this value and rerun the analysis.

  If hierarchical models are selected, only those terms that will keep the model hierarchical are candidates for addition or deletion. For example, the interaction term A*B will not be considered unless both A and B are already in the model. Likewise, the term A cannot be removed from a model that contains A*B.

Stop search when number of terms reaches

Once this number of terms has been entered into the model, the subset selection algorithm is terminated. Often you will have to run the procedure twice to find an appropriate value. You would set this value high for the first run and then reset it appropriately for the second run, depending upon the values of the log likelihood.

Note that the intercept is counted in this number.

Iteration Tab

This panel lets you control the maximum likelihood estimation algorithm.

Iteration Options

These options control the number of iterations used while the algorithm is searching for the maximum likelihood solution.

Maximum Iterations

This option specifies the maximum number of iterations used while finding a solution. If this number is reached, the procedure is terminated prematurely. This is used to prevent an infinite loop and to reduce the running time of lengthy variable selection runs.

Usually, no more the 20 iterations are needed. In fact, most runs converge in about 7 or 8 iterations.

During a variable selection run, it may be advisable reset this value to 4 or 5 to speed up the variable selection. Usually, the last few iterations make little difference in the estimated values of the regression coefficients.

Convergence Zero

This option specifies the convergence target for the maximum likelihood estimation procedure. The algorithm finds the maximum relative change of the regression coefficients. If this amount is less than the value set here, the maximum likelihood procedure is terminated.

For large datasets, you might want to increase this value to about 0.0001 so that fewer iterations are used, thus decreasing the running time of the procedure.

Regression Coefficient Starting Values

These options control the starting regression coefficient values (the B’s).

Start B’s at

Select a starting value (or enter a list of individual starting values) for the regression coefficients (the B’s).

Although the B’s can be any numeric value, the typical range is between -1 and 1. So starting values in this range usually allow the algorithm to converge to a useful solution.

The Cox regression algorithm solves for the maximum likelihood estimates of the regression coefficients by the iterative Newton-Raphson algorithm. This algorithm begins at a set of starting values for the regression coefficients and, at each iteration, modifies the B’s in a way that leads to a local maximum of the likelihood function. Sometimes the algorithm does not converge to the global maximum, so a different set of starting values must be tried.

Typically, a ‘good’ solution is one with all B’s less than 50 in absolute value. If your solution has one or more B’s that are large (over 10,000), you should rerun the algorithm with a different set of starting values.

List of Starting B’s (*If Start B’s at = “List”*)

Enter a list of starting values. If not enough values are entered, the last value will be used over and over.

Although the B's can be any numeric value, the typical range is between -1 and 1. So starting values in this range usually allow the algorithm to converge to a useful solution.

Reports Tab

The following options control which reports are displayed.

Alpha

Alpha Level

Alpha is the significance level used in the hypothesis tests. One minus alpha is the confidence level of the confidence intervals. A value of 0.05 is most commonly used. This corresponds to a chance of error of 1 in 20. You should not be afraid to use other values since 0.05 became popular in pre-computer days when it was the only value available.

Typical values range from 0.001 to 0.20.

Select Reports – Summary

Run Summary

Indicate whether to display this summary report.

Select Reports – Subset Selection

Subset Selection - Summary and Subset Selection - Detail

Indicate whether to display these subset selection reports.

Select Reports – Estimation

Regression Coefficients ... C.L. of Regression Coefficients

Indicate whether to display these estimation reports.

Select Reports – Goodness-of-Fit

Analysis of Deviance ... Baseline Hazard and Survival

Indicate whether to display these model goodness-of-fit reports.

Select Reports – Row-by-Row Lists

Residuals ... Predicted Values

Indicate whether to display these list reports. Note that since these reports provide results for each row, they may be too long for normal use when requested on large databases.

Order of Row Reports

This option specifies the order of the observations displayed on reports that display a separate value for each row. The rows can be displayed in the original order of the database or sorted by the time value, from lowest to highest.

Report Options Tab

The options on this panel control the label and decimal options of the report.

Variable Labels

Variable Names

This option lets you select whether to display only variable names, variable labels, or both.

Stagger label and output if label length is ≥

The names of the indicator variables can be too long to fit in the space provided. If the name contains more characters than the number specified here, only the name is shown on the first line of the report and the rest of the output is placed on the next line.

Enter *1* when you want the each variable's results printed on two lines.

Enter *100* when you want each variable's results printed on a single line.

Decimal Places

Precision

Specify the precision of numbers in the report. A single-precision number will show seven-place accuracy, while a double-precision number will show thirteen-place accuracy. Note that the reports are formatted for single precision. If you select double precision, some numbers may run into others. Also note that all calculations are performed in double precision regardless of which option you select here. This is for reporting purposes only.

Time ... Z or Chi^2 Decimals

These options specify the number of decimal places shown on the reports for the indicated values.

Plots Tab

These options control the attributes of the various plots.

Select Plots

Null Martingale Resid vs X Plot ... Deviance Resid vs Time Plot

Indicate whether to display these plots. Click the plot format button to change the plot settings.

Storage Tab

These options let you specify if, and where on the dataset, various statistics are stored.

Warning: Any data already in these columns are replaced by the new data. Be careful not to specify columns that contain important data.

Data Storage Options

Storage Option

This option controls whether the values indicated below are stored on the dataset when the procedure is run.

- **Do not store data**
  No data are stored even if they are checked.
- **Store in empty columns only**
  The values are stored in empty columns only. Columns containing data are not used for data storage, so no data can be lost.
- **Store in designated columns**
  Beginning at the *Store First Item In*, the values are stored in this column and those to the right. If a column contains data, the data are replaced by the storage values. Care must be used with this option because it cannot be undone.

Store First Variable In

The first item is stored in this column. Each additional item that is checked is stored in the columns immediately to the right of this column.

Leave this value blank if you want the data storage to begin in the first blank column on the right-hand side of the data.

Warning: any existing data in these columns is automatically replaced, so be careful.

Data Storage Options – Select Items to Store

Expanded X Values ... Covariance Matrix

Indicate whether to store these row-by-row values, beginning at the column indicated by the *Store First Item In* option. Note that several of these values include a different value for each covariate and so they require several columns when they are stored.

Expanded X Values

This option refers to the experimental design matrix. They include all binary and interaction variables generated.

Example 1 – Cox Regression Analysis

This section presents an example of how to run a Cox regression analysis. The data used are found in the LungCancer dataset. These data are an excerpt from a lung cancer study reported in Kalbfleisch (1980). The variables used in the analysis are

TIME	Days of survival
CENSOR	Censor indicator
STATUS	Karnofsky rating performance status
MONTHS	Months from diagnosis
AGE	Age in years
THERAPY	Prior therapy: 0 no, 10 yes

The purpose of this analysis is study the relationship between length of patient survival and the covariates. You may follow along here by making the appropriate entries or load the completed template **Example 1** by clicking on Open Example Template from the File menu of the Cox Regression window.

1 Open the LungCancer dataset.

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **LungCancer.NCSS**.
- Click **Open**.

2 Open the Cox Regression window.

- Using the Analysis menu or the Procedure Navigator, find and select the **Cox Regression** procedure.
- On the menus, select **File**, then **New Template**. This will load the default template.

3 Specify the variables.

- On the Cox Regression window, select the **Variables, Model tab**.
- Enter **Time** in the **Time** variable box.
- Set the **Ties Method** to **Efron**.
- Enter **Censor** in the **Censor** variable box.
- Enter **Status-Therapy** in the **Numeric X's** variables box.

4 Specify the reports.

- On the Cox Regression window, select the **Reports tab**.
- Check all of the reports. Although under normal circumstances you would not need all of the reports, we will view them all here so they can be annotated.

5 Run the procedure.

- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.

Run Summary

Parameter	Value	Parameter	Value
Rows Read	15	Time Variable	Time
Rows Filtered Out	0	Censor Variable	Censor
Rows Missing X's	0	Frequency Variable	None
Rows Processed	15	Subset Method	None
Rows Prediction Only	0	Ind. Var's Available	4
Rows Failed	13	No. of X's in Model	4
Rows Censored	2	Iterations	7
Sum of Frequencies	15	Maximum Iterations	20
Sum Censored Freqs	2	Convergence Criterion	1E-09
Sum Failed Freqs	13	Achieved Convergence	1.541585E-15
Final Log Likelihood	-20.1143	Completion Message	Normal completion
Starting B's	0		

This report summarizes the characteristics of the dataset and provides useful information about the reports to follow. It should be studied to make sure that the data were read in properly and that the estimation algorithm terminated normally. We will only discuss those parameters that need special explanation.

Rows Read

This is the number of rows processed during the run. Check this count to make certain it agrees with what you anticipated.

Iterations

This is the number of iterations used by the maximum likelihood procedure. This value should be compared against the value of the Maximum Iterations option to see if the iterative procedure terminated early.

Achieved Convergence

This is the maximum of the relative changes in the regression coefficients on the last iteration. If this value is less than the Convergence Criterion, the procedure converged normally. Otherwise, the specified convergence precision was not achieved.

Final Log Likelihood

This is the log likelihood of the model.

Regression Coefficients

Independent Variable	Regression Coefficient (B)	Standard Error of B	Risk Ratio Exp(B)	Mean	Wald Z-Value	Prob Level	Pseudo R2
B1 Status	-0.032415	0.020324	0.9681	57.3333	-1.5949	0.1107	0.2203
B2 Months	0.064557	0.033056	1.0667	12.6000	1.9530	0.0508	0.2975
B3 Age	0.039805	0.035232	1.0406	60.3333	1.1298	0.2586	0.1241
B4 Therapy	0.013967	0.068384	1.0141	4.6667	0.2042	0.8382	0.0046

Estimated Cox Regression Model

Exp(-0.0324152392634531*Status + 0.0645571159984993*Months + 0.0398048128120681*Age + 0.0139668973406698*Therapy)

This report displays the results of the proportional hazards estimation. Following are the detailed definitions:

Independent Variable

This is the variable from the model that is displayed on this line. If the variable is continuous, it is displayed directly. If the variable is discrete, the binary variable is given. For example, suppose that a discrete independent GRADE variable has three values: A, B, and C. The name shown here would be something like *GRADE=B*. This refers to a binary variable that is one for those rows in which GRADE was B and zero otherwise.

Note that the placement of the name is controlled by the *Stagger label and output* option of the Report Options tab.

Regression Coefficient (B)

This is the estimate of the regression coefficient, β_i. Remember that the basic regression equation is

$$\ln[h(T)] = \ln[h_0(T)] + \sum_{i=1}^{p} x_i \beta_i$$

Thus the quantity β_i is the amount that the log of the hazard rate changes when x_i is increased by one unit. Note that a positive coefficient implies that as the value of the covariate is increased, the hazard increases and the prognosis gets worse. A negative coefficient indicates that as the variable is increased, the hazard decreases and the prognosis gets better.

Standard Error

This is s_{b_j}, the large-sample estimate of the standard error of the regression coefficient. This is an estimate of the precision of the regression coefficient. It is provided by the square root of the corresponding diagonal element of the covariance matrix, $V(\hat{\beta}) = I^{-1}$. It is also used as the denominator of the Wald test.

Risk Ratio Exp(B)

This the value of e^{β_i}. This value is often called the *risk ratio* since it is the ratio of two hazards whose only difference is that x_i is increased by one unit. That is,

$$\frac{h(T \mid x_i = a+1)}{h(T \mid x_i = a)} = e^{\beta_i}$$

In this example, if Months is increased by one, the hazard rate is increased by 6.67%. If you want to calculate the affect of increasing Months by three, the hazard rate is increased by $1.0667^3 = 1.2137$, or 21.37%. Note that is not equal to 3.0 times 6.67.

Mean

This is the average of this independent variable. The means are especially important in interpreting the baseline hazard rates. Unless you have opted otherwise, the independent variables have been centered by subtracting these mean values. Hence, the baseline hazard rate occurs when each independent variable is equal to its mean.

Wald Z-Value

This is the *z* value of the Wald test used for testing the hypothesis that $\beta_i = 0$ against the alternative $\beta_i \neq 0$. The Wald test is calculated using the formula

$$z_i = \frac{b_{ij}}{s_{b_i}}$$

The distribution of the Wald statistic is closely approximated by the normal distribution in large samples. However, in small samples, the normal approximation may be poor. For small samples, likelihood ratio tests perform better and are preferred.

Prob Level

This is the two-sided probability level. This is the probability of obtaining a z-value larger in absolute value than the one obtained. If this probability is less than the specified significance level (say 0.05), the regression coefficient is significantly different from zero.

Pseudo R^2

An index value, similar to R^2 in regression, representing the relative influence of this variable. If $C = z^2$, n = sample size, and p = number of variables, then $R^2 = C/(n-p+C)$.

Estimated Cox Model

This section gives the Cox regression model in a regular text format that can be used as a transformation formula. The regression coefficients are displayed in double precision because a single-precision formula does not include the accuracy necessary to calculate the hazard rates.

Note that transformation must be less than 255 characters. Since these formulas are often greater than 255 characters in length, you must use the FILE(filename) transformation. To do so, copy the formula to a text file using Notepad, Windows Write, or Word to receive the model text. Be sure to save the file as an unformatted text (ASCII) file. The transformation is FILE(filename) where *filename* is the name of the text file, including directory information. When the transformation is executed, it will load the file and use the transformation stored there.

Confidence Limits

Independent Variable	Regression Coefficient (B)	Lower 95.0% Confidence Limit of B	Upper 95.0% Confidence Limit of B	Risk Ratio Exp(B)	Lower 95.0% C.L. of Exp(B)	Upper 95.0% C.L. of Exp(B)
B1 Status	-0.032415	-0.072250	0.007420	0.9681	0.9303	1.0074
B2 Months	0.064557	-0.000230	0.129345	1.0667	0.9998	1.1381
B3 Age	0.039805	-0.029249	0.108859	1.0406	0.9712	1.1150
B4 Therapy	0.013967	-0.120062	0.147996	1.0141	0.8869	1.1595

This report provides the confidence intervals for the regression coefficients and the risk ratios. The confidence coefficient, in this example 95%, was specified on the Format tab.

Independent Variable

This is the independent variable that is displayed on this line. If the variable is continuous, it is displayed directly. If the variable is discrete, the definition of the binary variable that was generated is given. For example, suppose that a discrete independent GRADE variable has three values: A, B, and C. The name shown here would be something like *GRADE=B*. This refers to a binary variable that is one for those rows in which GRADE was B and zero otherwise.

Note that the placement of the name is controlled by *Stagger label and output* option of the Report Options tab.

Regression Coefficient (B or Beta)

This is the estimate of the regression coefficient, β_i. Remember that the basic regression equation is

$$\ln\left[h(T)\right] = \ln\left[h_0(T)\right] + \sum_{i=1}^{p} x_i \beta_i$$

Thus the quantity β_i is the amount that the log of the hazard rate changes when x_i is increased by one unit. Note that a positive coefficient implies that as the value of the covariate is increased, the hazard increases and the prognosis gets worse. A negative coefficient indicates that as the variable is increased, the hazard decreases and the prognosis gets better.

Confidence Limits of B

A 95% confidence interval for β_i is given by an upper and lower limit. These limits are based on the Wald statistic using the formula

$$b_i \pm z_{1-\alpha/2} s_{b_i}$$

Since they are based on the Wald test, they are only valid for large samples.

Risk Ratio Exp(B)

This the value of e^{β_i}. This value is often called the *risk ratio* since it is the ratio of two hazards whose only difference is that x_i is increased by one unit. That is,

$$\frac{h(T \mid x_i = a+1)}{h(T \mid x_i = a)} = e^{\beta_i}$$

In this example, if Months is increased by one, the hazard rate is increased by 6.67%. If you want to calculate the affect of increasing Months by three, the hazard rate is increased by $1.0667^3 = 1.2137$, or 21.37%. Note that is not equal to 3.0 times 6.67.

Confidence Limits of Exp(B)

A 95% confidence interval for e^{β_i} is given by an upper and lower limit. These limits are based on the Wald statistic using the formula

$$\exp\left(b_i \pm z_{1-\alpha/2} s_{b_i}\right)$$

Since they are based on the Wald test, they are only valid for large samples.

Analysis of Deviance

Term(s) Omitted	DF	-2 Log Likelihood	Increase From Model Deviance (Chi²)	Prob Level
All Terms	4	46.6698	6.4413	0.1685
Status	1	42.7787	2.5501	0.1103
Months	1	44.3928	4.1642	0.0413
Age	1	41.5943	1.3657	0.2426
Therapy	1	40.2704	0.0419	0.8379
None(Model)	4	40.2286		

This report is the Cox regression analog of the analysis of variance table. It displays the results of a chi-square test used to test whether each of the individual terms in the regression are statistically significant after adjusting for all other terms in the model.

This report is not produced during a subset selection run.

Note that this report requires that a separate regression be run for each line. Thus, if the running time is too long, you might consider omitting this report.

Term Omitted

This is the model term that is being tested. The test is formed by comparing the deviance statistic when the term is removed with the deviance of the complete model. Thus, the deviance when the term is left out of the model is shown.

The “All” line refers to a no-covariates model. The “None(Model)” refers to the complete model with no terms removed.

Note that it is usually not advisable to include an interaction term in a model when one of the associated main effects is missing—which is what happens here. However, in this case, we believe this to be a useful test.

Note also that the name may become very long, especially for interaction terms. These long names may misalign the report. You can force the rest of the items to be printed on the next line by using the *Stagger label and output* option of the Report Options tab. This should create a better looking report when the names are extra long.

DF

This is the degrees of freedom of the chi-square test displayed on this line. DF is equal to the number of individual independent variables in the term.

Log Likelihood

This is the log likelihood achieved by the model being described on this line of the report.

R^2 of Remaining Terms

This is the difference between the deviance for the model described on this line and the deviance of the complete model. This value follows the chi^2 distribution in medium to large samples. This value can be thought of as the analog of the residual sum of squares in multiple regression. Thus, you can think of this value as the increase in the residual sum of squares that occurs when this term is removed from the model.

Another way to interpret this test is as a *redundancy test* because it tests whether this term is redundant after considering all of the other terms in the model.

Prob Level

This is the significance level of the chi^2 test. This is the probability that a chi^2 value with degrees of freedom DF is equal to this value or greater. If this value is less than 0.05 (or other appropriate value), the term is said to be statistically significant.

Log Likelihood & R^2 Section

Term(s) Omitted	DF	Log Likelihood	R^2 Of Remaining Term(s)	Reduction From Model R^2
All Terms	4	-23.3349	0.0000	0.3491
Status	1	-21.3893	0.2285	0.1206
Months	1	-22.1964	0.1408	0.2083
Age	1	-20.7971	0.2871	0.0620
Therapy	1	-20.1352	0.3473	0.0018
None(Model)	4	-20.1143	0.3491	0.0000

This report provides the log likelihoods and R^2 values of various models. This report is not produced during a subset selection run.

Note that this report requires that a separate Cox regression be run for each line. Thus, if the running time is too long, you might consider omitting this report.

Term Omitted

This is the term that is omitted from the model. The “All” line refers to no-covariates model. The “None(Model)” refers to the complete model with no terms removed. The “None(Model)” refers to the complete model with no terms removed.

Note that the name may become very long, especially for interaction terms. These long names may misalign the report. You can force the rest of the items to be printed on the next line by using the *Stagger label and output* option of the Report Options tab. This should create a better looking report when the names are extra long.

DF

This is the degrees of freedom of the term displayed on this line.

Log Likelihood

This is the log likelihood of the model displayed on this line. Note that this is the log likelihood of the logistic regression without the term listed.

R^2 of Remaining Term(s)

This is the R^2 of the model displayed on this line. Note that the model does not include the term listed at the beginning of the line. This R^2 is analogous to the R^2 in multiple regression, but it is not the same.

Hosmer and Lemeshow (1999) indicate that at the time of the writing of their book, there is no single, easy to interpret measure in Cox regression that is analogous to R^2 in multiple regression. They indicate that if such a measure "must be calculated" they would use

$$R_p^2 = 1 - \exp\left[\frac{2}{n}\left(L_0 - L_p\right)\right]$$

where L_0 is the log likelihood of the model with no covariates, n is the number of observations (censored or not), and L_p is the log likelihood of the model that includes the covariates.

Reduction From Model R^2

This is amount that R^2 is reduced when the term is omitted from the regression model. This reduction is calculated from the R^2 achieved by the full model.

This quantity is used to determine if removing a term causes a large reduction in R^2. If it does not, then the term can be safely removed from the model.

Baseline Cumulative Hazard & Survival Section

Time	Centered Baseline Cumulative Survival	Centered Baseline Cumulative Hazard	Alpha	Centered Baseline Hazard Rate
8	0.9654	0.0352	0.9654	0.0346
10	0.8912	0.1152	0.9232	0.0768
11	0.8183	0.2006	0.9181	0.0819
42	0.7449	0.2945	0.9103	0.0897
72	0.6717	0.3980	0.9017	0.0983
82	0.5934	0.5220	0.8834	0.1166
110	0.4942	0.7048	0.8329	0.1671
118	0.3904	0.9407	0.7898	0.2102
126	0.2911	1.2341	0.7457	0.2543
144	0.1843	1.6915	0.6330	0.3670
228	0.0922	2.3841	0.5003	0.4997
314	0.0288	3.5461	0.3128	0.6872
411	0.0288	3.5461	0.0000	1.0000

This report displays various estimated survival and hazard values. These are centered if the Centered X's option is selected.

Baseline Cumulative Survival

This estimates the cumulative survival probability of an individual with all covariates equal to their means or to zero depending on whether the data are centered or not. It is the value of $S_0(T)$ which is estimated using the formula

$$S_0(T) = \prod_{T_i \le T} \alpha_t$$

Baseline Cumulative Hazard

This estimates the cumulative baseline hazard of an individual with a set of covariates all equal to zero. It is the value of $H_0(T)$ which is calculated using the formula

$$H_0(T) = -\ln\left(S_0(T)\right)$$

Alpha

This is the value of the conditional baseline survival probabilities at the times listed. These values are used to calculate $S_0(T)$.

Baseline Hazard Rate

This is the estimate of the baseline hazard rates $h_0(T_t)$ which are calculated as follows

$$h_0(T_t) = 1 - \alpha_t$$

Residuals Report

Row	Time	Cox-Snell Residual		Martingale Residual		Deviance Residual	
12	8	1.3862	||||||.....	-0.3862	||.....	-0.3454	||.....
6	10	0.1411	|.....	0.8589	||||||.....	1.4828	||||||||||...
15	11	0.0791	|.....	0.9209	||||||.....	1.7978	||||||||||||
14+	25	0.0590	|.....	-0.0590	|.....	-0.3434	||.....
11	42	0.3307	|.....	0.6693	||||.....	0.9352	||||||.....
1	72	0.3364	|.....	0.6636	||||.....	0.9229	||||||.....
7	82	1.1774	|||||.....	-0.1774	|.....	-0.1679	|.....
10+	100	0.3112	|.....	-0.3112	|.....	-0.7890	||||||.....
8	110	1.2387	||||||.....	-0.2387	|.....	-0.2220	|.....
5	118	0.7300	|||.....	0.2700	|.....	0.2991	|.....
4	126	1.0748	|||||.....	-0.0748	|.....	-0.0730	|.....
13	144	2.4532	||||||||||...	-1.4532	|||||||||.....	-1.0543	|||||||.....
3	228	0.4531	||.....	0.5469	|||.....	0.6996	|||||.....
9	314	2.9953	||||||||||||||	-1.9953	||||||||||||||	-1.3403	||||||||||....
2	411	1.7951	||||||||.....	-0.7951	|||||.....	-0.6481	|||||.....

The various residuals were discussed in detail earlier in this chapter. Only a brief definition will be given were.

Row

This is the row from the database that is displayed on this line. Rows with a plus sign were censored.

Time

This is the value of the elapsed time.

Cox-Snell Residuals

Cox-Snell residuals were created to assess the goodness-of-fit of the Cox regression. They have since been replaced by other types of residuals and are now only of historical interest. See, for example, the discussion of Marubini and Valsecchi (1996) who state that the use of these residuals on distributional grounds should be avoided.

Martingale Residuals

The martingale residuals are defined as

$$M_t = c_t - r_t$$

where c_t is one if there is a failure at time T_t and zero otherwise. The martingale residual measures the difference between whether an individual experiences the event of interest and the expected number of events based on the model. The maximum value of the residual is one and the minimum possible value is negative infinity. Thus, the residual is highly skewed. A large negative martingale residual indicates a high risk individual who still had a long survival time.

Martingale residuals can not be used to assess goodness-of-fit as are the usual residuals in multiple regression. They have two main uses. First, they can be used to find outliers—individuals who are poorly fit by the model. Second, martingale residuals can be used to determine the functional form of each of the covariates in the model.

Martingale residuals can be used to determine the functional form of a covariate. To do this, you generate the Martingale residuals from a model without the covariate. Next, you plot these residuals against the value of the covariate.

Deviance Residuals

Deviance residuals are used to search for outliers. The deviance residuals are defined as

$$DEV_t = sign(M_t)\sqrt{-2[M_t + c_t \ln(c_t - M_t)]}$$

or zero when M_t is zero. These residuals are plotted against the risk scores given by

$$\exp\left(\sum_{i=1}^{p} x_{it} b_i\right)$$

When there is slight to moderate censoring, large absolute values in these residuals point to potential outliers. When there is heavy censoring, there will be a large number of residuals near zero. However, large absolute values will still indicate outliers.

Martingale Residuals

Row	Time	Null Martingale Residual		Martingale Residual	
12	8	0.9310	|||||||.....	-0.3862	||.....
6	10	0.8569	|||||||.....	0.8589	||||||.....
15	11	0.7769	|||||||.....	0.9209	||||||.....
14+	25	-0.2231	|.....	-0.0590	|.....
11	42	0.6815	||||||.....	0.6693	||||.....
1	72	0.5762	|||||.....	0.6636	||||.....
7	82	0.4584	|||.....	-0.1774	|.....
10+	100	-0.5416	||||.....	-0.3112	|.....
8	110	0.3043	||.....	-0.2387	|.....
5	118	0.1219	|.....	0.2700	|.....
4	126	-0.1012	|.....	-0.0748	|.....
13	144	-0.3889	|||.....	-1.4532	|||||||||.....
3	228	-0.7944	|||||||.....	0.5468	|||.....
9	314	-1.4875	|||||||||||||	-1.9953	|||||||||||||
2	411	-1.4875	|||||||||||||	-0.7951	|||||.....

The various residuals were discussed in detail earlier in this chapter. Only a brief definition will be given were.

Row

This is the row from the database that is displayed on this line. Rows with a plus sign were censored.

Time

This is the value of the elapsed time.

Null Martingale Residuals

These are the null martingale residuals. They are computed from a null (no covariate) model. Therneau and Grambsch (2000) suggest that the null-model martingale residuals can show the ideal functional form of the covariates so long as the covariates are not highly correlated among themselves. To find the appropriate functional form, each covariate is plotted against these residuals.

Martingale Residuals

The martingale residuals are repeated here. They were defined in the Residuals Section.

Schoenfeld Residuals

Schoenfeld Residuals

Row	Time	Resid Status		Resid Months		Resid Age	
12	8	-3.4327	|.....	11.8140	||||||||||...	-0.1121	|.....
6	10	-33.7298	||||||||||||||	-5.7472	|||||.....	-14.4483	||||||||||...
15	11	12.7982	||||.....	-0.3388	|.....	-16.9356	|||||||||||||
11	42	3.8458	|.....	-7.4120	||||||.....	15.1299	||||||||||..
1	72	4.2736	|.....	-5.2365	|||||.....	4.8130	||||.....
7	82	-15.3358	||||||.....	-2.7151	||.....	5.2528	||||.....
8	110	20.6225	||||||||.....	14.7012	|||||||||||||	6.6884	||||.....
5	118	18.4375	|||||||.....	2.2723	||.....	6.2230	||||.....
4	126	12.1419	||||.....	0.7288	|.....	5.4733	||||.....
13	144	-14.3230	||||||.....	-4.0590	||||.....	7.0669	||||||.....
3	228	2.1964	|.....	-8.8792	||||||||.....	-11.2819	||||||||.....
9	314	-7.4946	|||.....	4.8715	||||.....	-7.8693	||||||.....
2	411	0.0000	|.....	0.0000	|.....	0.0000	|.....

Schoenfeld Residuals

Row	Time	Resid Therapy	
12	8	1.5295	|||.....
6	10	-3.8822	||||||||.....
15	11	5.7181	|||||||||||..
11	42	-3.9309	||||||||.....
1	72	-4.3682	|||||||||.....
7	82	5.2326	||||||||||...
8	110	-3.3664	||||||.....
5	118	5.3579	||||||||||...
4	126	6.4343	|||||||||||||
13	144	-1.6923	|||.....
3	228	-3.2851	||||||.....
9	314	-3.7473	|||||||.....
2	411	0.0000	|.....

This report displays the Schoenfeld residuals for each noncensored individual. Note that most authors suggest using the scaled Schoenfeld residuals rather than these residuals. Since these residuals were discussed earlier in this chapter, only a brief definition will be given were.

Row

This is the row from the database that is displayed on this line. Rows with a plus sign were censored.

Time

This is the value of the elapsed time.

Schoenfeld Residuals

The Schoenfeld residuals are defined as follows

$$r_{it} = c_t \left[x_{it} - \sum_{r \in R_t} x_{ir} w_r \right]$$

where

$$w_r = \frac{\sum_{r \in R_t} x_{ir} \theta_r}{\sum_{r \in R_t} \theta_r}$$

Thus, this residual is the difference between the actual value of the covariate and a weighted average where the weights are determined from the risk scores. These residuals are used to estimate the influence of an observation on each of the regression coefficients. Plots of these quantities against the row number or against the corresponding covariate values are used to study these residuals.

Scaled Schoenfeld Residuals

Scaled Schoenfeld Residuals Section

Row	Time	Resid Status		Resid Months		Resid Age	
12	8	-0.0569	|||||.....	0.1828	||||||||||||	0.0276	|.....
6	10	-0.1280	|||||||||||||	-0.0528	||||.....	-0.1660	|||||||.....
15	11	0.0701	|||||||.....	-0.0731	|||||.....	-0.3476	|||||||||||||
11	42	0.0355	||||.....	-0.0812	||||||.....	0.2516	|||||||||.....
1	72	0.0487	||||.....	-0.0873	||||||.....	0.0959	||||.....
7	82	-0.1048	|||||||||||...	0.0410	|||.....	0.0482	||.....
8	110	0.0753	|||||||.....	0.1616	|||||||||||..	0.1586	|||||.....
5	118	0.0611	||||||.....	0.0237	|.....	0.0300	|.....
4	126	0.0280	|||.....	0.0206	|.....	0.0116	|.....
13	144	-0.0690	|||||||.....	-0.0020	|.....	0.1376	|||||.....
3	228	0.0663	||||||.....	-0.1822	||||||||||||.	-0.1832	||||||.....
9	314	-0.0262	|||.....	0.0489	||||.....	-0.0642	||.....
2	411	0.0000	|.....	0.0000	|.....	0.0000	|.....

Scaled Schoenfeld Residuals Section

Row	Time	Resid Therapy	
12	8	0.1550	|||||.....
6	10	0.0223	|.....
15	11	0.4537	|||||||||||||
11	42	-0.4288	||||||||||||.
1	72	-0.3501	|||||||||....
7	82	0.3223	||||||||.....
8	110	-0.2982	||||||||.....
5	118	0.1971	||||||.....
4	126	0.2903	||||||||.....
13	144	-0.1256	||||.....
3	228	-0.1361	||||.....
9	314	-0.1018	|||.....
2	411	0.0000	|.....

This report displays the scaled Schoenfeld residuals for each noncensored individual. These residuals are often used to find influential observations. Since these residuals were discussed earlier in this chapter, only a brief definition will be given were.

Row

This is the row from the database that is displayed on this line. Rows with a plus sign were censored.

Time

This is the value of the elapsed time.

Scaled Schoenfeld Residuals

The scaled Schoenfeld residuals are defined as follows

$$r_{kt}^{*} = m\sum_{i=1}^{p} V_{ik} r_{it}$$

where m is the total number of deaths in the dataset and V is the estimated covariance matrix of the regression coefficients. Hosmer and Lemeshow (1999) and Therneau and Grambsch (2000) suggest that scaling the Schoenfeld residuals by an estimate of their variance gives quantities with greater diagnostic ability. Hosmer and Lemeshow (1999) use the covariance matrix of the regression coefficients to perform the scaling.

These residuals are plotted against time to validate the proportional hazards assumption. If the proportional hazards assumption holds, the residuals will fall randomly around a horizontal line centered at zero. If the proportional hazards assumption does not hold, a trend will be apparent in the plot.

Predicted Values

Row	Time	Cumulative Baseline Hazard	Linear Predictor XB	Relative Risk Exp(XB)	Cumalitive Hazard H(T|X)	Cumulative Survival S(T|X)
12	8	0.0352	3.6734	39.3805	1.3861	0.2500
6	10	0.1152	0.2032	1.2254	0.1411	0.8684
15	11	0.2006	-0.9303	0.3944	0.0791	0.9239
14+	25	0.2006	-1.2244	0.2939	0.0590	0.9427
11	42	0.2945	0.1158	1.1228	0.3307	0.7184
1	72	0.3980	-0.1681	0.8452	0.3364	0.7143
7	82	0.5220	0.8135	2.2557	1.1774	0.3081
10+	100	0.5220	-0.5170	0.5963	0.3112	0.7325
8	110	0.7048	0.5640	1.7576	1.2387	0.2898
5	118	0.9407	-0.2536	0.7760	0.7300	0.4819
4	126	1.2341	-0.1382	0.8709	1.0748	0.3414
13	144	1.6915	0.3718	1.4503	2.4532	0.0860
3	228	2.3840	-1.6603	0.1901	0.4532	0.6356
9	314	3.5461	-0.1688	0.8447	2.9953	0.0500
2	411	3.5461	-0.6808	0.5062	1.7951	0.1661

This report displays various values estimated by the model. These are centered if the Centered X's option is selected.

Row

This is the row from the database that is displayed on this line. Rows with a plus sign were censored.

Time

This is the value of the elapsed time.

Baseline Cumulative Hazard

This estimates the cumulative baseline hazard of this individual. The baseline hazard occurs when all covariates are equal to zero (or to their means if centering is used). It is the value of $H_0(T)$ which is calculated using the formula

$$H_0(T) = -\ln(S_0(T))$$

Linear Predictor

This is the value of the linear portion of the Cox regression model. It is the logarithm of the ratio of the hazard rate to the baseline hazard rate. That is, it is the logarithm of the hazard ratio (or relative risk). The formula for the linear predictor is

$$\ln\left[\frac{h(T)}{h_0(T)}\right] = \sum_{i=1}^{p} x_i\beta_i$$

This value is occasionally suggested for use in plotting.

Relative Risk Exp(XB)

This is the ratio between the actual hazard rate and the baseline hazard rate, sometimes called the *risk ratio* or the *relative risk*. The formula for this quantity is

$$\frac{h(T)}{h_0(T)} = \exp\left(\sum_{i=1}^{p} x_i\beta_i\right) = e^{x_1\beta_1}e^{x_2\beta_2}\cdots e^{x_p\beta_p}$$

Cumulative Hazard H(T|X)

Under the proportional hazards regression model, the cumulative hazard is the sum of the individual hazard rates from time zero to time *T*.

$$\begin{aligned} H(T,X) &= \int_0^T h(u,X)du \\ &= \int_0^T h_0(u)e^{\sum_{i=1}^{p} x_i\beta_i} du \\ &= e^{\sum_{i=1}^{p} x_i\beta_i} \int_0^T h_0(u)du \\ &= H_0(T)e^{\sum_{i=1}^{p} x_i\beta_i} \end{aligned}$$

Note that the time survival time *T* is present in $H_0(T)$, but not in $e^{\sum_{i=1}^{p} x_i\beta_i}$. Hence, the cumulative hazard up to time *T* is represented in this model by a baseline cumulative hazard $H_0(T)$ which is adjusted for the covariates by multiplying by the factor $e^{\sum_{i=1}^{p} x_i\beta_i}$.

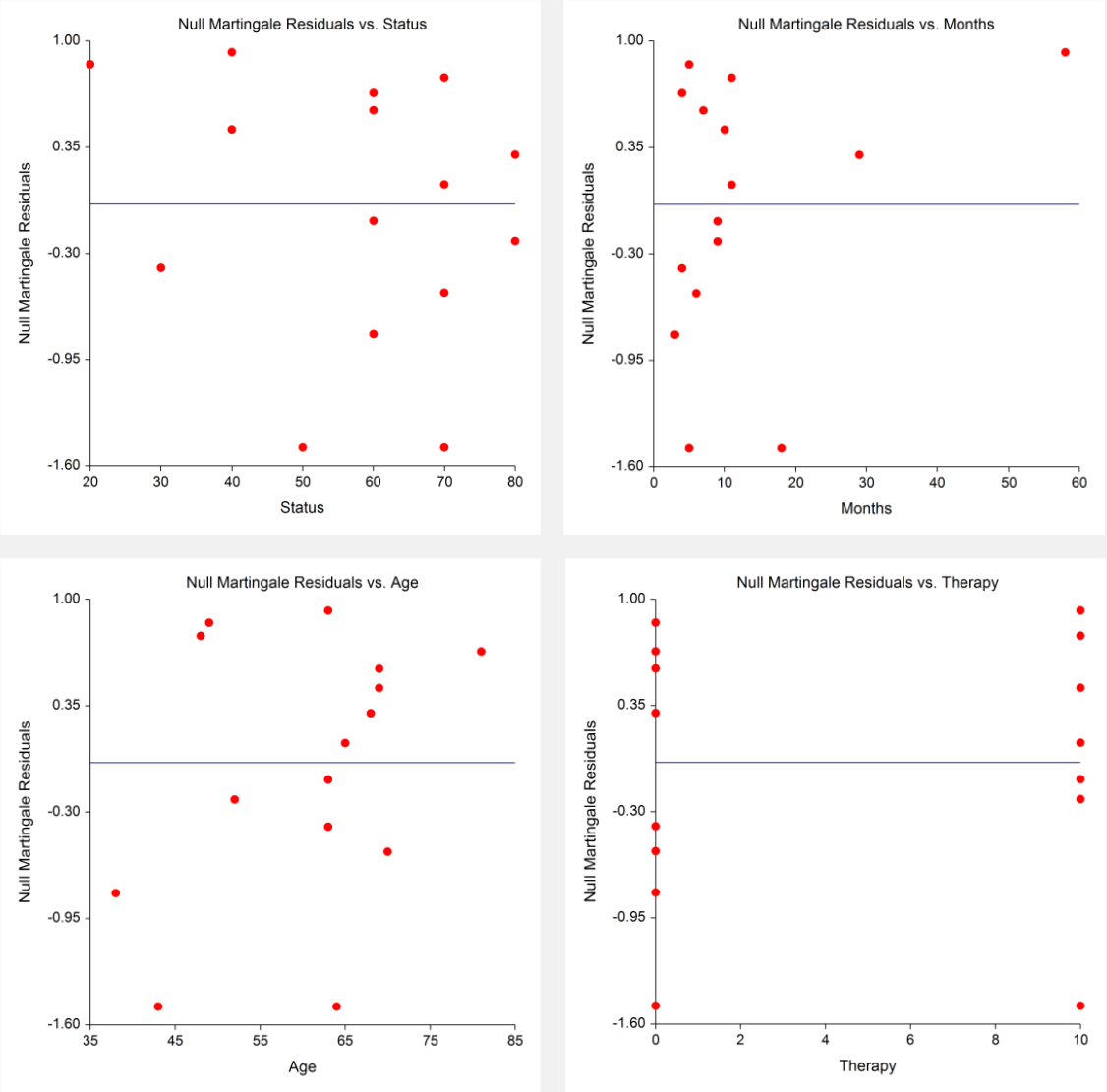
Cumulative Survival S(T|X)

Under the proportional hazards regression model, the cumulative survival is the probability that an individual survives past *T*. The formula for the cumulative survival is

$$\begin{aligned} S(T,X) &= \exp(-H(T,X)) \\ &= \exp\left(-H_0(T)e^{\sum_{i=1}^{p} x_i\beta_i}\right) \\ &= \left[e^{-H_0(T)}\right]^{e^{\sum_{i=1}^{p} x_i\beta_i}} \\ &= S_0(T)^{e^{\sum_{i=1}^{p} x_i\beta_i}} \end{aligned}$$

Note that the time survival time *T* is present in $S_0(T)$, but not in $e^{\sum_{i=1}^{p} x_i\beta_i}$.

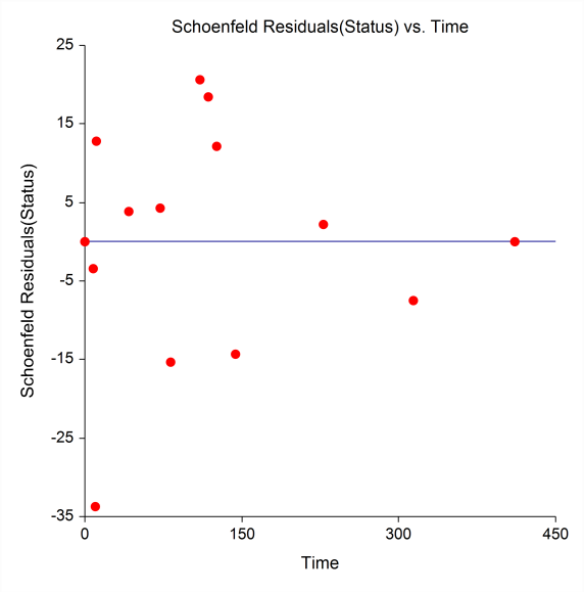
Null Martingale Residuals vs X's Plot(s)

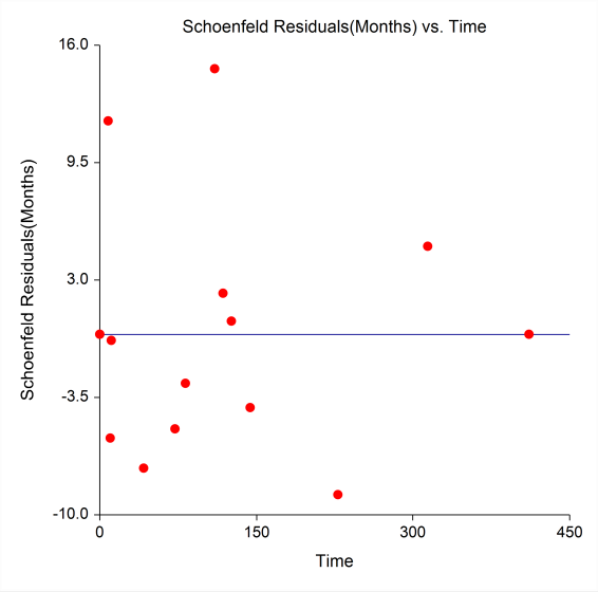


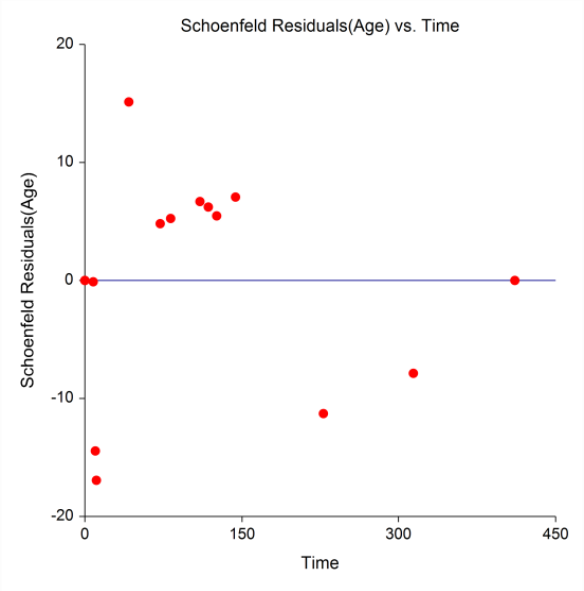
Each of the covariates are plotted against the null martingale residuals. If the covariates are not highly correlated, these plot will show the appropriate functional form of each covariate. A lowess curve and a regular least squares line are added to the plot to aid the eye. Ideally, the lowess curve will track along the least squares line. Be careful not to over interpret the ends of the lowess curves which are based on only a few individuals.

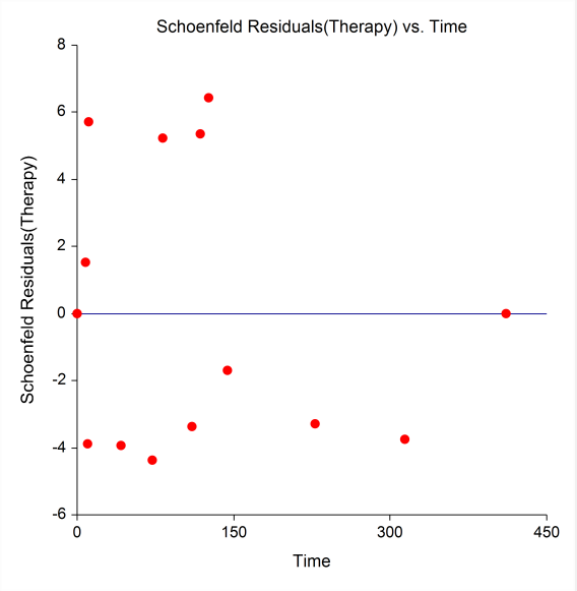
When curvature is present, you have to decide how the model should be modified to deal with it. You might need to add the square or the logarithm of the covariate to the model.

Schoenfeld Residuals vs Time Plot(s)







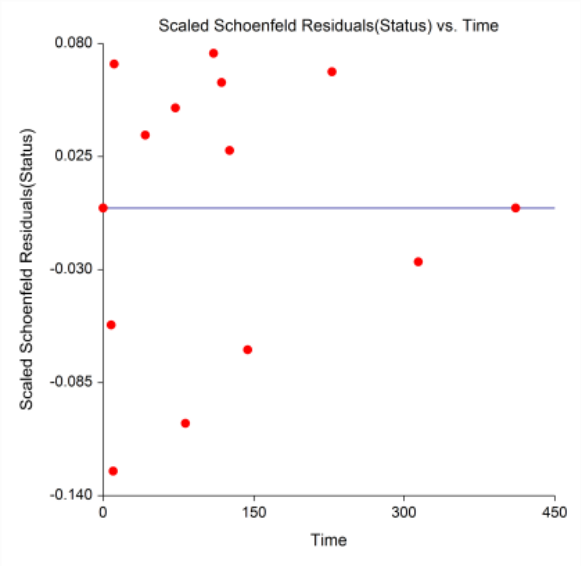


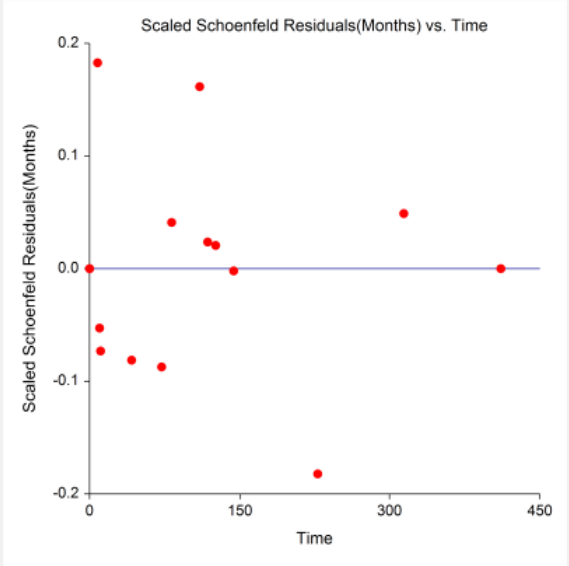
The Schoenfeld residuals are plotted for two reasons. First of all, these plots are useful in assessing whether the proportional hazards assumption is met. If the least squares line is horizontal and the lowess curve seems to track the least squares line fairly well, the proportional hazard assumption is reasonable.

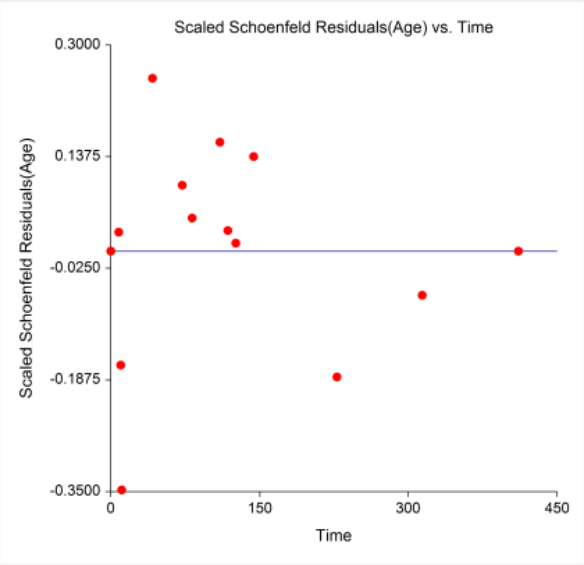
Second, points that are very influential in determining the estimated regression coefficient for a covariate show up as outliers on these plots. When influential points are found, it is important to make sure that the data associated with these points are accurate. It is not advisable to remove these influential points unless a specific reason can be found for doing so.

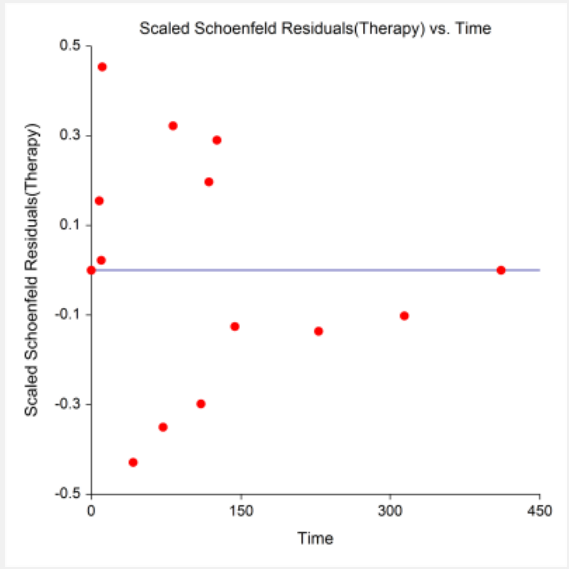
Many authors suggest that the scaled Schoenfeld residuals are more useful than these, unscaled, residuals.

Scaled Schoenfeld Residuals vs Time Plot(s)





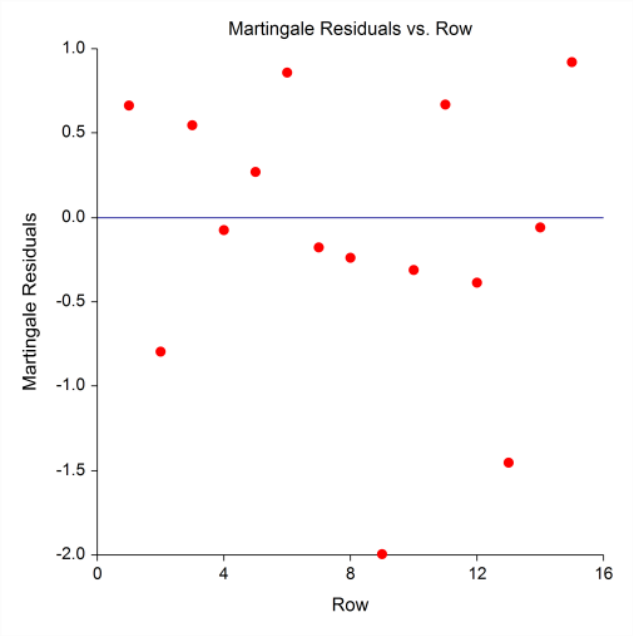




The scaled Schoenfeld residuals are plotted for two reasons. First of all, these plots are useful in assessing whether the proportional hazards assumption is met. If the least squares line is horizontal and the lowess curve seems to track the least squares line fairly well, the proportional hazard assumption is reasonable.

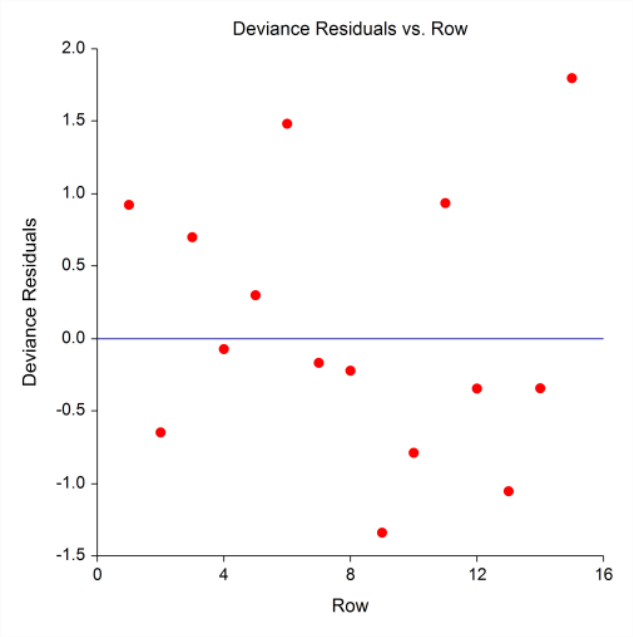
Second, points that are very influential in determining the estimated regression coefficient for a covariate show up as outliers on these plots. When influential points are found, it is important to make sure that the data associated with these points are accurate. It is not advisable to remove these influential points unless a specific reason can be found for doing so.

Martingale Residuals vs Row Plot



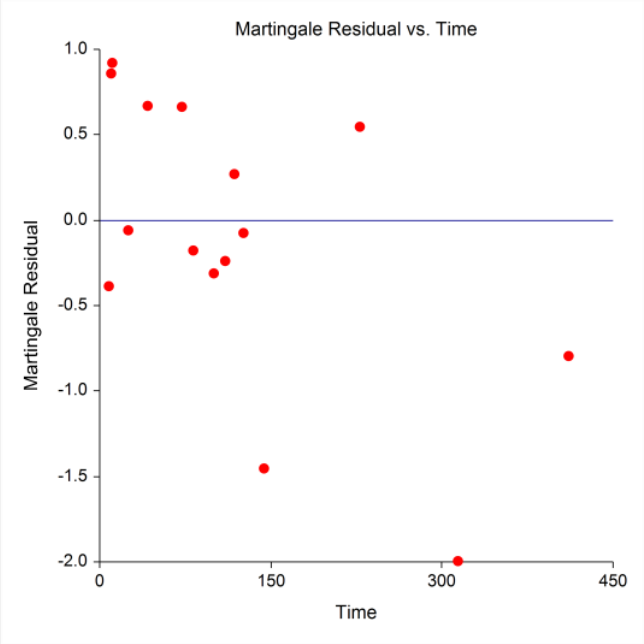
This plot allows you to find outliers. These outliers should be double-checked to be certain that the data are not in error. You should not routinely remove outliers unless you can find a good reason for doing so. Often, the greatest insight during an investigation comes while considering why these outliers are different.

Deviance Residuals vs Row Plot



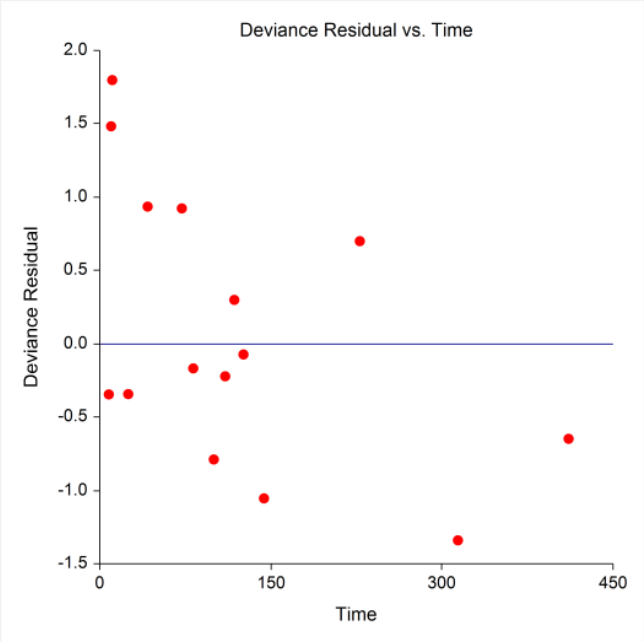
This plot allows you to find outliers. These outliers should be double-checked to be certain that the data are not in error. You should not routinely remove outliers unless you can find a good reason for doing so. Often, the greatest insight during an investigation comes while considering why these outliers are different.

Martingale Residuals vs Time Plot



This plot allows you to find outliers. These outliers should be double-checked to be certain that the data are not in error. You should not routinely remove outliers unless you can find a good reason for doing so. Often, the greatest insight during an investigation comes while considering why these outliers are different.

Deviance Residuals vs Time Plot



This plot allows you to find outliers. These outliers should be double-checked to be certain that the data are not in error. You should not routinely remove outliers unless you can find a good reason for doing so. Often, the greatest insight during an investigation comes while considering why these outliers are different.

Example 2 – Subset Selection

This section presents an example of how to conduct a subset selection. We will again use the LungCancer dataset that was used in Example 1. In this run, we will be trying to find a subset of the covariates that should be kept in the regression model.

You may follow along here by making the appropriate entries or load the completed template **Example 2** by clicking on Open Example Template from the File menu of the Cox Regression window.

1 Open the LungCancer dataset.

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **LungCancer.NCSS**.
- Click **Open**.

2 Open the Cox Regression window.

- Using the Analysis menu or the Procedure Navigator, find and select the **Cox Regression** procedure.
- On the menus, select **File**, then **New Template**. This will load the default template.

3 Specify the variables.

- On the Cox Regression window, select the **Variables, Model tab**.
- Enter **Time** in the **Time** box.
- Set the **Ties Method** to **Efron**.
- Enter **Censor** in the **Censor Variable** box.
- Enter **Status-Therapy** in the **Numeric X's** box.

4 Specify the Subset Selection.

- Set the **Search Method** box to **Hierarchical Forward with Switching**.

5 Specify the reports.

- On the Cox Regression window, select the **Reports tab**.
- Uncheck all of the reports except **Subset Selection – Summary** and **Subset Selection - Detail**.

6 Run the procedure.

- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.

Subset Selection Summary Section

Number of Terms	Number of X's	Log Likelihood	R^2 Value	R^2 Change
0	0	-23.3349	0.0000	0.0000
1	1	-21.8803	0.1763	0.1763
2	2	-21.0354	0.2641	0.0878
3	3	-20.1352	0.3473	0.0832
4	4	-20.1143	0.3491	0.0018

This report shows the best log-likelihood value for each subset size. In this example, it appears that a model with three terms provides the best model. Note that adding the fourth variable does not increase the R-squared value very much.

No. Terms

The number of terms.

No. X's

The number of X's that were included in the model. Note that in this case, the number of terms matches the number of X's. This would not be the case if some of the terms were categorical variables.

Log Likelihood

This is the value of the log likelihood function evaluated at the maximum likelihood estimates. Our goal is to find a subset size above which little is gained by adding more variables.

R^2 Value

This is the value of R^2 calculated using the formula

$$R_k^2 = 1 - \exp\left[\frac{2}{n}\left(L_0 - L_k\right)\right]$$

as discussed in the introduction. We are looking for the subset size after which this value does not increase by a meaningful amount.

R^2 Change

This is the increase in R^2 that occurs when each new subset size is reached. Search for the subset size below which the R^2 value does not increase by more than 0.02 for small samples or 0.01 for large samples.

In this example, the optimum subset size appears to be three terms.

Subset Selection Detail Section

Step	Action	No. of Terms	No. of X's	Log Likelihood	R^2	Term Entered	Terms Removed
1	Begin	0	0	-23.3349	0.0000		
2	Add	1	1	-21.8803	0.1763	Months	
3	Add	2	2	-21.0354	0.2641	Status	
4	Add	3	3	-20.1352	0.3473	Age	
5	Add	4	4	-20.1143	0.3491	Therapy	

This report shows the highest log likelihood for each subset size. In this example, it appears that three terms provide the best model. Note that adding THERAPY does not increase the R-squared value very much.

Action

This item identifies the action that was taken at this step. A term was added, removed, or two were switched.

No. Terms

The number of terms.

No. X's

The number of X's that were included in the model. Note that in this case, the number of terms matches the number of X's. This would not be the case if some of the terms were categorical variables.

Log Likelihood

This is the value of the log likelihood function after the completion of this step. Our goal is to find a subset size above which little is gained by adding more variables.

R^2 Value

This is the value of R^2 calculated using the formula

$$R_k^2 = 1 - \exp\left[\frac{2}{n}\left(L_0 - L_k\right)\right]$$

as discussed in the introduction. We are looking for the subset size after which this value does not increase by a meaningful amount.

Terms Entered and Removed

These columns identify the terms added, removed, or switched.

Discussion of Example 2

After considering these reports, it was decided to include AGE, MONTHS, and STATUS in the final regression model. Another run is performed using only these independent variables. A complete residual analysis would be necessary before the equation is finally adopted.

Regression Coefficients Section

Independent Variable	Regression Coefficient (B)	Standard Error of B	Risk Ratio Exp(B)	Mean	Wald Z-Value	Prob Level	Pseudo R^2
Age	0.041940	0.033413	1.0428	60.3333	1.2552	0.2094	0.1361
Months	0.063724	0.032004	1.0658	12.6000	1.9912	0.0465	0.2838
Status	-0.031482	0.019680	0.9690	57.3333	-1.5997	0.1097	0.2037

This report displays the results of the proportional hazards estimation. Note that the Wald tests indicate that only Months is statistically significant. Because of the small sample size of this example and because they add a great deal to the R-squared value, we have added Age and Status to the final model.

Example 3 – Cox Regression with Categorical Variables

This example will demonstrate the analysis of categorical independent variables. A study was conducted to evaluate the influence on survival time of three variables: Age, Gender, and Treatment. The ages of the study participants were grouped into three age categories: 20, 40, and 60. The first age group (20) was selected as the reference group. The female group was selected as the reference group for Gender. The Treatment variable represented three groups: a control and two treatment groups. The control group was selected as the reference group for Treatment. The data for this study are contained in the **CoxReg** dataset.

You may follow along here by making the appropriate entries or load the completed template **Example 3** by clicking on Open Example Template from the File menu of the Cox Regression window.

1 Open the CoxReg dataset.

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **CoxReg.NCSS**.
- Click **Open**.

2 Open the Cox Regression window.

- Using the Analysis menu or the Procedure Navigator, find and select the **Cox Regression** procedure.
- On the menus, select **File**, then **New Template**. This will load the default template.

3 Specify the variables.

- On the Cox Regression window, select the **Variables, Model tab**.
- Enter **Time** in the **Time** box.
- Set the **Ties Method** to **Efron**.
- Enter **Status** in the **Censor Variable** box.
- Enter **Count** in the **Frequency Variable** box.
- Enter **Treatment Age Gender** in the **Categorical X's** box.

4 Specify the model.

- Set **Terms** to **Up to 2-Way**.

5 Specify the reports.

- On the Cox Regression window, select the **Reports tab**.
- Check the **Run Summary**, **Regression Coefficients**, **C.L. of Regression Coefficients**, **Analysis of Deviance**, and **Log-Likelihood and R^2** reports.

6 Run the procedure.

- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.

Run Summary

Parameter	Value	Parameter	Value
Rows Read	73	Time Variable	Time
Rows Filtered Out	0	Censor Variable	Status
Rows Missing X's	0	Frequency Variable	Count
Rows Processed	73	Subset Method	None
Rows Prediction Only	0	Ind. Var's Available	3
Rows Failed	54	No. of X's in Model	13
Rows Censored	19	Iterations	6
Sum of Frequencies	137	Maximum Iterations	20
Sum Censored Freqs	83	Convergence Criterion	1E-09
Sum Failed Freqs	54	Achieved Convergence	5.363288E-16
Final Log Likelihood	-222.9573	Completion Status	Normal completion
Starting B's	0		

This report summarizes the characteristics of the dataset. Note that 137 individuals were included in this study of which 83 were censored.

Regression Coefficients

Independent Variable	Regression Coefficient (B)	Standard Error of B	Risk Ratio Exp(B)	Mean	Wald Z-Value	Prob Level	Pseudo R2
B1 (Treatment="T1")	0.315769	0.707474	1.3713	0.3358	0.4463	0.6554	0.0044
B2 (Treatment="T2")	0.606087	0.674007	1.8332	0.3212	0.8992	0.3685	0.0177
B3 (Age=40)	0.178527	0.720145	1.1955	0.3066	0.2479	0.8042	0.0014
B4 (Age=60)	0.747377	0.652733	2.1115	0.3431	1.1450	0.2522	0.0283
B5 (Gender="M")	0.199655	0.629734	1.2210	0.5182	0.3170	0.7512	0.0022
B6 (Treatment="T1")*(Age=40)	-0.228646	0.872282	0.7956	0.1095	-0.2621	0.7932	0.0015
B7 (Treatment="T1")*(Age=60)	-0.124997	0.851308	0.8825	0.1022	-0.1468	0.8833	0.0005
B8 (Treatment="T2")*(Age=40)	-0.442119	0.843234	0.6427	0.0876	-0.5243	0.6001	0.0061
B9 (Treatment="T2")*(Age=60)	-1.726851	0.885161	0.1778	0.1168	-1.9509	0.0511	0.0780
B10 (Treatment="T1")*(Gender="M")	-0.976831	0.714997	0.3765	0.1752	-1.3662	0.1719	0.0398
B11 (Treatment="T2")*(Gender="M")	-0.553592	0.721736	0.5749	0.1606	-0.7670	0.4431	0.0129
B12 (Age=40)*(Gender="M")	0.420448	0.701899	1.5226	0.1679	0.5990	0.5492	0.0079
B13 (Age=60)*(Gender="M")	0.366048	0.709829	1.4420	0.1971	0.5157	0.6061	0.0059

This report displays the results of the proportional hazards estimation. Note that the names of the interaction terms are too long to fit in the space allotted, so the rest of the information appears on the next line.

Independent Variable

It is important to understand the variable names of the interaction terms. For example, consider the term: (Treatment=“T2”)*(Gender=“M”). This variable was created by multiplying two indicator variables. The first indicator is “1” when the treatment is “T2” and “0” otherwise. The second indicator is “1” when the gender is “M” and “0” otherwise. This portion of the gender-by-treatment interaction is represented by the product of these two variables.

The rest of the definitions are the same as before and so they are not repeated here.

Confidence Limits

Independent Variable	Regression Coefficient (B)	Lower 95.0% Confidence Limit of B	Upper 95.0% Confidence Limit of B	Risk Ratio Exp(B)	Lower 95.0% C.L. of Exp(B)	Upper 95.0% C.L. of Exp(B)
B1 (Treatment="T1")	0.315769	-1.070855	1.702392	1.3713	0.3427	5.4871
B2 (Treatment="T2")	0.606087	-0.714943	1.927116	1.8332	0.4892	6.8697
B3 (Age=40)	0.178527	-1.232933	1.589986	1.1955	0.2914	4.9037
B4 (Age=60)	0.747377	-0.531956	2.026709	2.1115	0.5875	7.5891
B5 (Gender="M")	0.199655	-1.034602	1.433911	1.2210	0.3554	4.1951
B6 (Treatment="T1")*(Age=40)	-0.228646	-1.938287	1.480996	0.7956	0.1440	4.3973
B7 (Treatment="T1")*(Age=60)	-0.124997	-1.793530	1.543536	0.8825	0.1664	4.6811
B8 (Treatment="T2")*(Age=40)	-0.442119	-2.094827	1.210589	0.6427	0.1231	3.3555
B9 (Treatment="T2")*(Age=60)	-1.726851	-3.461735	0.008033	0.1778	0.0314	1.0081
B10 (Treatment="T1")*(Gender="M")	-0.976831	-2.378199	0.424538	0.3765	0.0927	1.5289
B11 (Treatment="T2")*(Gender="M")	-0.553592	-1.968169	0.860985	0.5749	0.1397	2.3655
B12 (Age=40)*(Gender="M")	0.420448	-0.955248	1.796145	1.5226	0.3847	6.0264
B13 (Age=60)*(Gender="M")	0.366048	-1.025192	1.757288	1.4420	0.3587	5.7967

This report provides the confidence intervals for the regression coefficients and the risk ratios. The confidence coefficient, in this example 95%, was specified on the Format tab. Note that the names of the interaction terms are too long to fit in the space allotted, so the rest of the information appears on the next line.

Independent Variable

It is important to understand the variable names of the interaction terms. For example, consider the term: (Treatment=“T2”)*(Gender=“M”). This variable was created by multiplying two indicator variables. The first indicator is “1” when the treatment is “T2” and “0” otherwise. The second indicator is “1” when the gender is “M” and “0” otherwise. This portion of the gender-by-treatment interaction is represented by the product of these two variables.

The rest of the definitions are the same as before and so they are not repeated here.

Analysis of Deviance Section

Term(s) Omitted	DF	-2 Log Likelihood	Increase From Model Deviance (Chi^2)	Prob Level
All Terms	13	454.5022	8.5876	0.8033
Treatment	2	446.7191	0.8044	0.6688
Age	2	447.2661	1.3515	0.5088
Gender	1	446.0147	0.1001	0.7517
Treatment*Age	4	451.1965	5.2819	0.2596
Treatment*Gender	2	447.7827	1.8681	0.3930
Age*Gender	2	446.3421	0.4275	0.8076
None(Model)	13	445.9146		

This report is the Cox regression analog of the analysis of variance table. It displays the results of a chi-square test used to test whether each of the individual terms are statistically significant after adjusting for all other terms in the model.

The DF (degrees of freedom) column indicates the number of binary variables needed to represent each term. The chi^2 test is used to test the significance of all binary variables associated with a particular term.

Log Likelihood & R^2 Section

Term(s) Omitted	DF	Log Likelihood	R^2 Of Remaining Term(s)	Reduction From Model R^2
All Terms	13	-227.2511	0.0000	0.0608
Treatment	2	-223.3595	0.0552	0.0055
Age	2	-223.6331	0.0514	0.0093
Gender	1	-223.0074	0.0601	0.0007
Treatment*Age	4	-225.5982	0.0238	0.0369
Treatment*Gender	2	-223.8914	0.0479	0.0129
Age*Gender	2	-223.1711	0.0578	0.0029
None(Model)	13	-222.9573	0.0608	0.0000

This report displays the Log Likelihood and R^2 that is achieved when each term is omitted from the regression model. The DF (degrees of freedom) column indicates the number of binary variables needed to represent each term. The chi^2 test is used to test the significance of all binary variables associated with a particular term.

Example 4 – Validation of Cox Regression using Collett (1994)

Collett (1994), pages 156 and 157, present a dataset giving the results of a small study about kidney dialysis. This dataset contains two independent variables: Age and Sex. These data are contained in the NCSS dataset called Collett157.

Collett (1994) gives the estimated regression coefficients as 0.030 for Age and -2.711 for Sex. The chi-square test for Sex is 6.445 and the chi-square test for Age is 1.320. The Cox-Snell residual for the first patient is 0.3286. The martingale residual for this patient is 0.6714. The deviance residual for this patient is 0.9398. The Schoenfeld residuals for this patient are -1.0850 and -.2416.

We will run these data through NCSS and check that we obtain the same values. You may follow along here by making the appropriate entries or load the completed template **Example 4** by clicking on Open Example Template from the File menu of the Cox Regression window.

1 Open the Collett157 dataset.

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **Collett157.NCSS**.
- Click **Open**.

2 Open the Cox Regression window.

- Using the Analysis menu or the Procedure Navigator, find and select the **Cox Regression** procedure.
- On the menus, select **File**, then **New Template**. This will load the default template.

3 Specify the variables.

- On the Cox Regression window, select the **Variables, Model tab**.
- Enter **Time** in the **Time** box.
- Set the **Ties Method** to **Efron**.
- Enter **Status** in the **Censor** box.
- Enter **Age Sex** in the **Numerical X's** box.

4 Specify the reports.

- On the Cox Regression window, select the **Reports tab**.
- Check the **Run Summary**, **Regression Coefficients**, **Analysis of Deviance**, **Residuals**, and **Schoenfeld Residuals** reports.

5 Run the procedure.

- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.

Validation Report

Regression Coefficients Section

Independent Variable	Regression Coefficient (B)	Standard Error of B	Risk Ratio Exp(B)	Mean	Wald Z-Value	Prob Level	Pseudo R^2
B1 Age	0.030371	0.026237	1.0308	31.4615	1.1576	0.2470	0.1181
B2 Sex	-2.710762	1.095898	0.0665	1.7692	-2.4736	0.0134	0.3795

Analysis of Deviance Section

Term(s) Omitted	DF	-2 Log Likelihood	Increase From Model Deviance (Chi^2)	Prob Level
All Terms	2	40.9454	6.4779	0.0392
Age	1	35.7880	1.3204	0.2505
Sex	1	40.9132	6.4456	0.0111
None(Model)	2	34.4676		

Residuals Section

Row	Time	Cox-Snell Residual		Martingale Residual		Deviance Residual	
1	8	0.3286	|.....	0.6714	||||.....	0.9398	||||.....
2	15	0.0785	|.....	0.9215	|||||||.....	1.8020	|||||||||||||
3	22	1.4331	|||||||.....	-0.4331	|.....	-0.3828	|.....
4	24	0.0939	|.....	0.9061	|||||||.....	1.7087	||||||||||||.
5	30	1.7736	|||||||||.....	-0.7736	|||||.....	-0.6334	||.....
6+	54	0.3117	|.....	-0.3117	|.....	-0.7895	||||.....
7	119	0.2655	|.....	0.7345	|||||.....	1.0877	||||||.....
8	141	0.5386	||.....	0.4614	||.....	0.5611	|.....
9	185	1.6523	|||||||||.....	-0.6523	||||.....	-0.5480	|.....
10	292	1.4234	|||||||.....	-0.4234	|.....	-0.3751	|.....
11	402	1.4207	|||||||.....	-0.4207	|.....	-0.3730	|.....
12	447	2.3927	|||||||||||||	-1.3927	|||||||||||||	-1.0201	|||||.....
13	536	1.5640	||||||||.....	-0.5640	|||.....	-0.4832	|.....

Schoenfeld Residuals Section

Row	Time	Resid Age		Resid Sex	
1	8	-1.0850	|.....	-0.2416	||||.....
2	15	14.4930	||||||||||...	0.6644	|||||||||||||
3	22	3.1291	||.....	-0.3065	|||||.....
4	24	-10.2215	|||||||.....	0.4341	||||||||.....
5	30	-16.5882	||||||||||..	-0.5504	||||||||||...
7	119	-17.8286	|||||||||||||	0.0000	|.....
8	141	-7.6201	|||||.....	0.0000	|.....
9	185	17.0910	||||||||||||.	0.0000	|.....
10	292	10.2390	|||||||.....	0.0000	|.....
11	402	2.8575	||.....	0.0000	|.....
12	447	5.5338	||||.....	0.0000	|.....
13	536	0.0000	|.....	0.0000	|.....

You can verify that are results matched those of Collett (1994) within rounding.