SURVIVAL Example #2

SUDAAN Statements and Results Illustrated

- Cox proportional hazards model
- TIES option
- WALDCHI (Wald chi-square test) option
- SATADJCHI (Satterthwaite-adjusted chi-square test) option
- EFFECTS

Input Data Set(s): EXERCISE.SAS7bdat

Example

Consider a cross-over clinical trial with multivariate failure time data and evaluate the regression effect of treatment, after adjusting for covariates.

Solution

This example demonstrates SUDAAN's correlated data techniques in the context of a clinical trial. The data reported by Crouchley and Pickles (1993) for this example represent repeated exercise times to angina pectoris (in seconds) in patients with coronary heart disease. Refer to ***Section 12.2*** for a description of the study design and ***Exhibit 3*** for the structure of the data.

Exhibit 1. Structure of the Angina Pectoris Exercise Data

Patient ID	Treatment Day	Time Since Drug Admin (Hours)	Y = Exercise Time (seconds)	MI
1	Placebo Day	Pre-Dosing	150	1
1		1 hr post	172	1
1		3 hrs post	118	1
1		5 hrs post	143	1
1	Treatment Day	Pre-Dosing	136	1
1		1 hr post	445	1
1		3 hrs post	393	1
1		5 hrs post	226	1
2	Placebo Day	Pre-Dosing	205	0
2		1 hr post	287	0
2		3 hrs post	211	0
2		5 hrs post	207	0
2	Treatment Day	Pre-Dosing	250	0
2		1 hr post	306	0
2		3 hrs post	206	0
2		5 hrs post	224	0

Data consist of 168 records (21 patients, 8 records per patient).

The Cox proportional hazards model was used to evaluate the regression effect of treatment (test day), after adjusting for several covariates: time since drug administration (4-level factor), and indicators for previous myocardial infarction (MI), previous coronary artery bypass surgery (CAB), and previous propranolol treatment (PP). Treatment day and time since drug administration are within-cluster covariates, while MI, PP, and CAB represent cluster-level covariates.

To implement the cluster sample methods using SUDAAN, we estimated the model parameters under a standard partial likelihood and applied a robust variance estimator (labeled *Robust* in ***Exhibit 2***). The Wald chi-square test was used to evaluate the null hypothesis of no treatment effect. For comparison, the same proportional hazards model was also fit assuming complete independence of the response times (labeled *Naïve* in ***Exhibit 2***).

Exhibit 2 contains the robust vs. naïve results for the main effects model. Note that for the parameters that represent cluster-level covariates, the cluster sample method results in a substantial increase in standard errors. However, for within-cluster covariates (*e.g.*, the treatment and time effects), the cluster variance estimates are substantially smaller than the independence estimates. Using the design effect results of Neuhaus and Segal (1993) and proceeding by analogy to failure time data, the large observed design effects for the cluster-level covariates (*e.g.*, previous bypass surgery) indicate large response intracluster correlations. In this situation, the variance of the regression coefficients for such covariates is increased. However, the observed design effects for within-cluster covariates whose patterns do not vary from cluster to cluster (time since drug administration and treatment day) were much less than one (as low as 0.30), which would be expected when the response intracluster correlation is positive and the covariate intracluster correlation is negative. In this case, variance estimates for the regression coefficients would be smaller than that expected under independence, corresponding to a gain in efficiency.

As seen in ***Exhibit 2***, tests for treatment effects and time since drug administration were statistically significant under the cluster sample and independence approaches, but were slightly more significant under the cluster sample approach. Using cluster sample techniques, SUDAAN reports the estimated hazard ratio for treatment vs. control in the main effects only model to be 0.43, with a 95% confidence interval of (0.32 - 0.59). A hazard ratio less than 1.0 indicates longer exercise times in the treatment group (a protective effect against angina pectoris). The time-specific hazard ratios from the interaction model suggest that the treatment differences are largest at 1- and 3-hours post-dosing. In fact, SUDAAN reports a significant interaction effect between treatment day and time since drug administration (p=0.0204, Wald chi-square test). The estimated hazard ratios at 1- and 3-hours post-dosing are 0.22 and 0.35, respectively; and the hazard ratios at pre-dosing and 5-hours post-dosing are 0.67 and 0.53, respectively.

Tests for the cluster-level covariates (previous MI, bypass surgery, and propranolol treatment) became less significant under the cluster sample approach, and only previous myocardial infarction remained statistically significant in each of the three models due to the large design effects.

Exhibit 2. Proportional Hazards Regression, Exercise Time Data Main Effects Model

Covariate	Model-Fitting Method	Beta	S.E.	Design Effect[1]	Z	P-Value
Treatment Day (Treatment vs. Placebo)	Robust Naive	-0.8395 -0.8395	0.1474 0.1724	0.73 1.00	-5.70 -4.87	.0000 .0000
Time Since Drug Administration						
1 hour	Robust Naive	-0.9295 -0.9295	0.2085 0.2417	0.74 1.00	-4.46 -3.85	.0002 .0002
3 hours	Robust Naive	-0.6040 -0.6040	0.1294 0.2311	0.31 1.00	-4.67 -2.61	.0001 .0090
5 hours	Robust Naive	-0.1827 -0.1827	0.1216 0.2232	0.30 1.00	-1.50 -0.82	.1487 .4130
Previous MI	Robust Naive	-1.2263 -1.2263	0.3636 0.2004	3.29 1.00	-3.37 -6.12	.0030 .0000
Previous Bypass Surgery	Robust Naive	0.7525 0.7525	0.4025 0.1970	4.17 1.00	1.87 3.82	.0762 .0000
Previous Propranolol Treatment	Robust Naïve	-0.6282 -0.6282	0.4737 0.2182	4.71 1.00	-1.33 -2.88	.1998 .0040

Note:

In this example number of clusters = 21 and the cluster size = 2 days X 4 times each day = 8.

[1] Design Effect $= \left(\frac{SE_{Robust}}{SE_{Naive}} \right)^2$.

SUDAAN code for two proportional hazards models are contained in the following output:

- ***Exhibit 3*** contains the **interaction model**, containing the main effects of treatment day; time since drug administration (modeled as a 4-level categorical variable corresponding to pre-dosing, 1-hour, 3-hours, and 5-hours post-dosing); and the three continuous covariates MI, CAB, and PP; and the interaction effects between treatment and time since drug administration. In this model we also evaluate the simple effects of treatment at each of the four times since drug administration (EFFECTS statement).
- ***Exhibit 11*** contains the **main effects model**, and it included the main effects only. The results from the main effects model are included in ***Exhibit 2***.

In the SUDAAN code to fit the Cox proportional hazards model to the observed event times, the default sample design option DESIGN=WR (shorthand notation for "with replacement sampling") invokes the robust variance estimator that is appropriate for the study. The NEST statement in SUDAAN indicates that the patient (PATIENT) represents the cluster or primary sampling unit, with the keyword _ONE_ indicating that there is a single design stratum. Additional sources of intracluster correlation (such as time within each study day) need not be specified.

The requested test statistics WALDCHI and SATADJCHI refer to the usual Wald chi-square test and the Satterthwaite-adjusted chi-square test (Rao and Scott, 1987), respectively. The latter test is a modification of the usual Wald statistic and has been shown to have superior operating characteristics for multiple-degree-of-freedom hypotheses in small samples (Thomas and Rao, 1987).

This example handles ties using the Breslow method, using the option TIES= BRESLOW on the MODEL statement. This was the default in releases of SUDAAN 8 and earlier.

Exhibit 3. SAS-Callable SUDAAN Code for SURVIVAL: Interaction Model

```
libname in "c:\11winbetatest\examples";

options nocenter linesize=95 pagesize=60;

proc format;
  value hrs 1="1 hr"
            2="3 hrs"
            3="5 hrs"
            4="Pre-Dosing";
  value trt 1="Treatment Day"
            2="Placebo Day";

PROC SURVIVAL DATA=in.EXERCISE FILETYPE=SAS EPSILON=0.0001;
  NEST _ONE_ PATIENT;
  WEIGHT _ONE_;

  CLASS HRS SUDTRT;
  EVENT COMPLETE;
  MODEL EXTIME = SUDTRT HRS SUDTRT*HRS MI CAB PP / TIES=BRESLOW;
  EFFECTS SUDTRT=(1 -1) / HRS=1 NAME="1 Hr: Trt vs Placebo" EXP;
  EFFECTS SUDTRT=(1 -1) / HRS=2 NAME="3 Hrs: Trt vs Placebo" EXP;
  EFFECTS SUDTRT=(1 -1) / HRS=3 NAME="5 Hrs: Trt vs Placebo" EXP;
  EFFECTS SUDTRT=(1 -1) / HRS=4 NAME="Pre-Dosing: Trt vs Placebo" EXP;
  TEST WALDCHI SATADJCHI;

  SETENV COLSPCE=1 COLWIDTH=7 DECWIDTH=4 LABWIDTH=28;
  PRINT beta sebeta deft t_beta p_beta / tests=default t_betafmt=f6.2
        deftfmt=f6.2 waldchifmt=f6.2 satadchifmt=f7.2 dffmt=f7.0 satadjdffmt=f7.2;

  SETENV COLSPCE=3 COLWIDTH=5 DECWIDTH=3 LABWIDTH=30;
  PRINT / risk=default expcntrst=default hrfmt=f7.3 exp_cntrstfmt=f13.3;

  RFORMAT sudtrt trt.;
  RFORMAT hrs hrs.;
  RTITLE  "EXERCISE TIME TO ANGINA PECTORIS (SECONDS):  PLACEBO VS. TREATMENT"
          " "
          "PROPORTIONAL HAZARDS REGRESSION USING ROBUST VARIANCE ESTIMATOR"
          " "  "Interaction Model";
  RFOOTNOTE "Source:  Crouchley and Pickles (1993, Biometrics 49, 1067-1076)";
```

The interaction model contains the main effects of treatment (SUDTRT), time (HRS), and various covariates, as well as the term SUDTRT*HRS. It also contains EFFECTS statements to evaluate the treatment effect at each hour.

Exhibit 4. First Page of SURVIVAL Results (*.lst file)

```
                                S U D A A N
           Software for the Statistical Analysis of Correlated Data
         Copyright     Research Triangle Institute      December 2011
                               Release 11.0.0

DESIGN SUMMARY: Variances will be computed using the Taylor Linearization Method, Assuming a
With Replacement (WR) Design
    Sample Weight: _ONE_
    Stratification Variables(s): _ONE_
    Primary Sampling Unit: PATIENT

NOTE: Using a default start time of -10000000000 for all records

Number of observations read       :    168    Weighted count:      168
Observations used in the analysis :    168    Weighted count:      168
Denominator degrees of freedom    :     20

Maximum number of estimable parameters for the model is 10


Summary of Event Values
-------------------------------------------------------
COMPLETE                     Frequency      Weighted Sum
-------------------------------------------------------
Censored                        13.000            13.000
Non-Censored                   155.000           155.000
-------------------------------------------------------

SURVIVAL has converged to a solution in 5 iterations.

-2 * Normalized Log-Likelihood with Beta(s) = 0 :  1331.24
-2 * Normalized Log-Likelihood Full Model       :  1236.63
Approximate Chi-Square (-2 * Log-L Ratio)       :    94.61
Degrees of Freedom                              :       10
Approximate P-Value                             :     0.00

Note: The approximate Chi-Square is not adjusted for clustering.
      Refer to hypothesis test table for adjusted test.
```

This first table displays the number of observations read, used in analysis, denominator degrees of freedom, and the number of censored and non-censored times.

Exhibit 5. Frequencies for CLASS Variable HRS

```
Frequencies and Values for CLASS Variables
----------------------------------------
Hours Since
  Drug Admin    Frequency         Value
----------------------------------------
Ordered
  Position:
  1                    42          1 hr
Ordered
  Position:
  2                    42         3 hrs
Ordered
  Position:
  3                    42         5 hrs
Ordered
  Position:
  4                    42    Pre-Dosing
----------------------------------------
```

Exhibit 6. Frequencies for CLASS Variable SUDTRT

Frequencies and Values for CLASS Variables

Day	Frequency	Value
Ordered Position: 1	84	Treatment Day
Ordered Position: 2	84	Placebo Day

Exhibit 7. Regression Coefficients: Interaction Model

Variance Estimation Method: Taylor Series (WR)
Dependent Variable: EXTIME: Exercise Time to Angina Pectoris
Censoring Variable: COMPLETE
Ties Handling: BRESLOW

EXERCISE TIME TO ANGINA PECTORIS (SECONDS): PLACEBO VS. TREATMENT

PROPORTIONAL HAZARDS REGRESSION USING ROBUST VARIANCE ESTIMATOR

Interaction Model

Independent Variables and Effects	Beta Coeff.	SE Beta	DEFF Beta #4	T-Test B=0	P-value T-Test B=0
Hours Since Drug Admin					
1 hr	-0.4634	0.2013	0.42	-2.30	0.0322
3 hrs	-0.3399	0.1325	0.18	-2.57	0.0185
5 hrs	-0.0877	0.1137	0.13	-0.77	0.4495
Pre-Dosing	0.0000	0.0000	.	.	.
Day					
Treatment Day	-0.4056	0.1330	0.18	-3.05	0.0063
Placebo Day	0.0000	0.0000	.	.	.
Previous MI	-1.2397	0.3701	3.38	-3.35	0.0032
Previous Bypass Surgery	0.7362	0.4037	4.18	1.82	0.0832
Previous Propranolol Trt	-0.6152	0.4846	4.91	-1.27	0.2189
Hours Since Drug Admin, Day					
1 hr, Treatment Day	-1.1076	0.4130	0.72	-2.68	0.0143
1 hr, Placebo Day	0.0000	0.0000	.	.	.
3 hrs, Treatment Day	-0.6393	0.2515	0.30	-2.54	0.0194
3 hrs, Placebo Day	0.0000	0.0000	.	.	.
5 hrs, Treatment Day	-0.2286	0.1957	0.19	-1.17	0.2567
5 hrs, Placebo Day	0.0000	0.0000	.	.	.
Pre-Dosing, Treatment Day	0.0000	0.0000	.	.	.
Pre-Dosing, Placebo Day	0.0000	0.0000	.	.	.

Source: Crouchley and Pickles (1993, Biometrics 49, 1067-1076)

The regression coefficients table indicates that the interaction effect is likely to be significant, as two of its associated regression coefficients are significant. Standard errors and statistical tests are adjusted for clustering via the robust variance estimator.

Exhibit 8. ANOVA Table and User-Specified Contrasts: Interaction Model

Variance Estimation Method: Taylor Series (WR)
Dependent Variable: EXTIME: Exercise Time to Angina Pectoris
Censoring Variable: COMPLETE
Ties Handling: BRESLOW

EXERCISE TIME TO ANGINA PECTORIS (SECONDS): PLACEBO VS. TREATMENT

PROPORTIONAL HAZARDS REGRESSION USING ROBUST VARIANCE ESTIMATOR

Interaction Model

Contrast	Degrees of Freedom	S_waite Adj DF	S_waite Adj ChiSq	P-value S_waite ChiSq	Wald ChiSq	P-value Wald ChiSq
OVERALL MODEL	10	3.98	20.81	0.0003	44.84	0.0000
HRS	.	.	.	.	.	.
SUDTRT	.	.	.	.	.	.
MI	1	1.00	11.22	0.0008	11.22	0.0008
CAB	1	1.00	3.32	0.0683	3.32	0.0683
PP	1	1.00	1.61	0.2043	1.61	0.2043
HRS * SUDTRT	3	1.80	10.35	0.0044	9.80	0.0204
1 Hr: Trt vs Placebo	1	1.00	16.23	0.0001	16.23	0.0000
3 Hrs: Trt vs Placebo	1	1.00	19.05	0.0000	19.05	0.0000
5 Hrs: Trt vs Placebo	1	1.00	13.55	0.0002	13.55	0.0002
Pre-Dosing: Trt vs Placebo	1	1.00	9.30	0.0023	9.30	0.0023

Source: Crouchley and Pickles (1993, Biometrics 49, 1067-1076)

The ANOVA table indicates that the interaction effect is significant (p=0.0204 Wald chi-square), as well as the treatment effects at each hour.

Exhibit 9. Default Hazard Ratios: Interaction Model

Variance Estimation Method: Taylor Series (WR)
Dependent Variable: EXTIME: Exercise Time to Angina Pectoris
Censoring Variable: COMPLETE
Ties Handling: BRESLOW

EXERCISE TIME TO ANGINA PECTORIS (SECONDS): PLACEBO VS. TREATMENT

PROPORTIONAL HAZARDS REGRESSION USING ROBUST VARIANCE ESTIMATOR

Interaction Model

Independent Variables and Effects	Hazards Ratio	Lower 95% Limit	Upper 95% Limit
Hours Since Drug Admin			
1 hr	0.629	0.413	0.957
3 hrs	0.712	0.540	0.938
5 hrs	0.916	0.723	1.161
Pre-Dosing	1.000	1.000	1.000
Day			
Treatment Day	0.667	0.505	0.880
Placebo Day	1.000	1.000	1.000
Previous MI	0.289	0.134	0.626
Previous Bypass Surgery	2.088	0.899	4.847
Previous Propranolol Trt	0.541	0.197	1.485
Hours Since Drug Admin, Day			
1 hr, Treatment Day	0.330	0.140	0.782
1 hr, Placebo Day	1.000	1.000	1.000
3 hrs, Treatment Day	0.528	0.312	0.892
3 hrs, Placebo Day	1.000	1.000	1.000
5 hrs, Treatment Day	0.796	0.529	1.197
5 hrs, Placebo Day	1.000	1.000	1.000
Pre-Dosing, Treatment Day	1.000	1.000	1.000
Pre-Dosing, Placebo Day	1.000	1.000	1.000

Source: Crouchley and Pickles (1993, Biometrics 49, 1067-1076)

The default hazard ratios from an interaction model may not be the ones of interest. See the user-specified hazard ratios in the next exhibit.

Exhibit 10. User-Specified Hazard Ratios: Interaction Model

```
Variance Estimation Method: Taylor Series (WR)
Dependent Variable: EXTIME: Exercise Time to Angina Pectoris
Censoring Variable: COMPLETE
Ties Handling: BRESLOW
EXERCISE TIME TO ANGINA PECTORIS (SECONDS):  PLACEBO VS. TREATMENT

PROPORTIONAL HAZARDS REGRESSION USING ROBUST VARIANCE ESTIMATOR

Interaction Model
-----------------------------------------------------------------
Exponentiated Contrast                            Lower   Upper
                                                  95%     95%
                                 EXP(Contrast)    Limit   Limit
-----------------------------------------------------------------
1 Hr: Trt vs Placebo                      0.220   0.101   0.482
3 Hrs: Trt vs Placebo                     0.352   0.213   0.580
5 Hrs: Trt vs Placebo                     0.530   0.370   0.760
Pre-Dosing: Trt vs Placebo                0.667   0.505   0.880
-----------------------------------------------------------------
Source:  Crouchley and Pickles (1993, Biometrics 49, 1067-1076)
```

The EXP option on the EFFECTS statement produced the hazard ratios for treatment vs. placebo at each hour, which is of primary interest. Results indicate that being in the treatment group significantly reduces the hazard for the event (angina pectoris) at each hour, but most noticeably at 1 hr (0.220) and 3 hrs (0.352) post-dosing. This quantitative difference in hazard ratios yielded the significant interaction shown earlier.

Exhibit 11. SAS-Callable SUDAAN Code for SURVIVAL: Main Effects Model

```
PROC SURVIVAL DATA=in.EXERCISE FILETYPE=SAS EPSILON=0.0001;
  NEST _ONE_ PATIENT;
  WEIGHT _ONE_;

  CLASS HRS SUDTRT;
  EVENT COMPLETE;
  MODEL EXTIME = SUDTRT HRS MI CAB PP / TIES=BRESLOW;
  EFFECTS MI CAB PP / NAME="Combined Effect: MI, CAB, PP";
  TEST WALDCHI SATADJCHI;

  SETENV COLSPCE=1 COLWIDTH=7 DECWIDTH=4 LABWIDTH=28;
  PRINT beta sebeta deft t_beta p_beta / tests=default t_betafmt=f6.2 deftfmt=f6.2
        waldchifmt=f6.2 satadchifmt=f7.2 dffmt=f7.0 satadjdffmt=f7.2;

  SETENV COLSPCE=3 COLWIDTH=5 DECWIDTH=3 LABWIDTH=30;
  PRINT / risk=default hrfmt=f7.3;
  RFORMAT sudtrt trt.;
  RFORMAT hrs hrs.;
  RTITLE  "EXERCISE TIME TO ANGINA PECTORIS (SECONDS):  PLACEBO VS. TREATMENT"
          " "
          "PROPORTIONAL HAZARDS REGRESSION USING ROBUST VARIANCE ESTIMATOR"
          " "  "Main Effects Model";
  RFOOTNOTE "Source:  Crouchley and Pickles (1993, Biometrics 49, 1067-1076)";
```

The main effects model contains the main effects of treatment (SUDTRT), time (HRS), and various covariates. Results from this main effects model are contained in ***Exhibit 2***.

Exhibit 12. First Page of SURVIVAL Results (*.lst file)

```
                                S U D A A N
           Software for the Statistical Analysis of Correlated Data
         Copyright     Research Triangle Institute      December 2011
                              Release 11.0.0


DESIGN SUMMARY: Variances will be computed using the Taylor Linearization Method, Assuming a
With Replacement (WR) Design
    Sample Weight: _ONE_
    Stratification Variables(s): _ONE_
    Primary Sampling Unit: PATIENT


NOTE: Using a default start time of -10000000000 for all records

Number of observations read       :    168    Weighted count:      168
Observations used in the analysis :    168    Weighted count:      168
Denominator degrees of freedom    :     20


Maximum number of estimable parameters for the model is  7



Summary of Event Values
-----------------------------------------------------------
COMPLETE                      Frequency      Weighted Sum
-----------------------------------------------------------
Censored                         13.000            13.000
Non-Censored                    155.000           155.000
-----------------------------------------------------------

SURVIVAL has converged to a solution in 5 iterations.

-2 * Normalized Log-Likelihood with Beta(s) = 0 :  1331.24
-2 * Normalized Log-Likelihood Full Model       :  1242.68
Approximate Chi-Square (-2 * Log-L Ratio)       :    88.56
Degrees of Freedom                              :        7
Approximate P-Value                             :     0.00

Note: The approximate Chi-Square is not adjusted for clustering.
      Refer to hypothesis test table for adjusted test.
```

This first table displays the number of observations read, used in analysis, denominator degrees of freedom, and the number of censored and non-censored times.

Exhibit 13. Regression Coefficients: Main Effects Model

Variance Estimation Method: Taylor Series (WR)
Dependent Variable: EXTIME: Exercise Time to Angina Pectoris
Censoring Variable: COMPLETE
Ties Handling: BRESLOW
EXERCISE TIME TO ANGINA PECTORIS (SECONDS): PLACEBO VS. TREATMENT

PROPORTIONAL HAZARDS REGRESSION USING ROBUST VARIANCE ESTIMATOR

Main Effects Model

Independent Variables and Effects	Beta Coeff.	SE Beta	DEFF Beta #4	T-Test B=0	P-value T-Test B=0
Hours Since Drug Admin					
1 hr	-0.9295	0.2085	0.74	-4.46	0.0002
3 hrs	-0.6040	0.1294	0.31	-4.67	0.0001
5 hrs	-0.1827	0.1216	0.30	-1.50	0.1487
Pre-Dosing	0.0000	0.0000	.	.	.
Day					
Treatment Day	-0.8395	0.1474	0.73	-5.70	0.0000
Placebo Day	0.0000	0.0000	.	.	.
Previous MI	-1.2263	0.3636	3.29	-3.37	0.0030
Previous Bypass Surgery	0.7525	0.4025	4.17	1.87	0.0762
Previous Propranolol Trt	-0.6282	0.4737	4.71	-1.33	0.1998

Source: Crouchley and Pickles (1993, Biometrics 49, 1067-1076)

The regression coefficients table indicates that the treatment effect is significant (p=0.0000). Standard errors and statistical tests are adjusted for clustering via the robust variance estimator. The design effect describes the impact of clustering on the variance of the regression coefficients.

Exhibit 14. ANOVA Table and User-Specified Contrasts: Main Effects Model

Variance Estimation Method: Taylor Series (WR)
Dependent Variable: EXTIME: Exercise Time to Angina Pectoris
Censoring Variable: COMPLETE
Ties Handling: BRESLOW
EXERCISE TIME TO ANGINA PECTORIS (SECONDS): PLACEBO VS. TREATMENT

PROPORTIONAL HAZARDS REGRESSION USING ROBUST VARIANCE ESTIMATOR

Main Effects Model

Contrast	Degrees of Freedom	S_waite Adj DF	S_waite Adj ChiSq	P-value S_waite ChiSq	Wald ChiSq	P-value Wald ChiSq
OVERALL MODEL	7	3.57	20.57	0.0003	49.58	0.0000
HRS	3	2.29	30.73	0.0000	31.22	0.0000
SUDTRT	1	1.00	32.43	0.0000	32.43	0.0000
MI	1	1.00	11.37	0.0007	11.37	0.0007
CAB	1	1.00	3.50	0.0616	3.50	0.0615
PP	1	1.00	1.76	0.1848	1.76	0.1848
Combined Effect: MI, CAB, PP	3	2.86	13.17	0.0037	15.43	0.0015

Source: Crouchley and Pickles (1993, Biometrics 49, 1067-1076)

The ANOVA table indicates that the treatment effect is significant (p=0.0000), as well as the effects of time (HRS) and MI.

Exhibit 15. Default Hazard Ratios: Main Effects Model

Variance Estimation Method: Taylor Series (WR)
Dependent Variable: EXTIME: Exercise Time to Angina Pectoris
Censoring Variable: COMPLETE
Ties Handling: BRESLOW
EXERCISE TIME TO ANGINA PECTORIS (SECONDS): PLACEBO VS. TREATMENT

PROPORTIONAL HAZARDS REGRESSION USING ROBUST VARIANCE ESTIMATOR

Main Effects Model

Independent Variables and Effects	Hazards Ratio	Lower 95% Limit	Upper 95% Limit
Hours Since Drug Admin			
1 hr	0.395	0.256	0.610
3 hrs	0.547	0.417	0.716
5 hrs	0.833	0.646	1.074
Pre-Dosing	1.000	1.000	1.000
Day			
Treatment Day	0.432	0.318	0.587
Placebo Day	1.000	1.000	1.000
Previous MI	0.293	0.137	0.626
Previous Bypass Surgery	2.122	0.917	4.914
Previous Propranolol Trt	0.534	0.199	1.433

Source: Crouchley and Pickles (1993, Biometrics 49, 1067-1076)

Results indicate that being in the treatment group significantly reduces the hazard for the event by more than half (HR = .432), averaged over hour and the other covariates.