**Conduct Backward Selection in Multivariable Firth’s penalized partial likelihood Cox regression mode**

**Macro:** %FirthPhreg\_sel

**Created Date/Author:** Apr 04, 2018/Chao Zhang, and Yuan Liu

**Current Version**: V1

**Working Environment:** SAS 9.4 English version

Cox models probably lead to biased estimation of regression coefficients when survival dataset has too few outcome events.

The phenomenon of monotone likelihood occurs in the fitting process of a Cox model when at least one parameter estimation

diverges to ±∞. Firth’s penalized partial likelihood Cox regression mode to analyze survival dataset with rare events.

**Purpose**: To conduct backward selection on a Firth’s penalized partial likelihood approach in Cox regression models, and a table of the resulting model can be generated.

**Notes:** The model runs using PROC PHREG. The macro “MULTIPLE\_PHREGFirth V1” or later is also required.

**Reference**: macros on FineGray\_Sel V4, and GENMOD\_SEL V1

**Parameters:**

|  |  |
| --- | --- |
| **Macro variable** | **Description** |
| DSN | The name of the data set to be analyzed. |
| EVENT | Name of time to event outcome variable. |
| CENSOR | Name of censoring indicator variable. Values of 0 indicate censored. |
| VAR | The list of variables on interest in the initial model that would be eliminated during the backward selection procedure separated by spaces. The order of variables in this list will be preserved in the final report. |
| CVAR | The list of categorical variables that are in VAR and FORCEINVAR. If need to change the reference group, you can follow each variable name by (DESC) or by (ref = “Ref level in formatted value”) where needed and separate terms by \*. See code example. |
| INC | Number of variables to include in the model (optional). The first n variables in the var parameter will be included in every model. The default value is 0. |
| ALPHA | The significance level for removing variables from the model (optional). The default value is .2. |
| REPORT | Set it to T if a results summary table is desired. Otherwise check Log for variable selected by the backward elimination. |
| TYPE3 | Set to F to suppress type III p-values from being reported in the table (optional). The default value is T. This only has an effect if REPORT = T. |
| CLNUM | Set to T if you want to see the number of observations for each level of covariates. The default is T. |
| ORIENTATION | Orientation of the output Word table. Default is portrait, can be changed to landscape. |
| FILENAME | File name for output table. This is necessary if report=T. |
| OUTPATH | File path for output table to be stored. This is necessary if report=T. |
| DEBUG | Set to T if running in debug mode (optional). Work datasets will not be deleted in debug mode. This is useful if you are editing the code or want to further manipulate the resulting data sets. The default value is F. |

**Usage Example:**

**data** Myeloma;

input Time VStatus LogBUN hgb Platelet Age LogWBC Frac

LogPBM Protein SCalc;

label Time='Survival Time'

VStatus='0=Alive 1=Dead';

datalines;

1.25 1 2.2175 9.4 1 67 3.6628 1 1.9542 12 10

1.25 1 1.9395 12.0 1 38 3.9868 1 1.9542 20 18

2.00 1 1.5185 9.8 1 81 3.8751 1 2.0000 2 15

2.00 1 1.7482 11.3 0 75 3.8062 1 1.2553 0 12

2.00 1 1.3010 5.1 0 57 3.7243 1 2.0000 3 9

3.00 1 1.5441 6.7 1 46 4.4757 0 1.9345 12 10

5.00 1 2.2355 10.1 1 50 4.9542 1 1.6628 4 9

5.00 1 1.6812 6.5 1 74 3.7324 0 1.7324 5 9

6.00 1 1.3617 9.0 1 77 3.5441 0 1.4624 1 8

6.00 1 2.1139 10.2 0 70 3.5441 1 1.3617 1 8

6.00 1 1.1139 9.7 1 60 3.5185 1 1.3979 0 10

6.00 1 1.4150 10.4 1 67 3.9294 1 1.6902 0 8

7.00 1 1.9777 9.5 1 48 3.3617 1 1.5682 5 10

7.00 1 1.0414 5.1 0 61 3.7324 1 2.0000 1 10

7.00 1 1.1761 11.4 1 53 3.7243 1 1.5185 1 13

9.00 1 1.7243 8.2 1 55 3.7993 1 1.7404 0 12

11.00 1 1.1139 14.0 1 61 3.8808 1 1.2788 0 10

11.00 1 1.2304 12.0 1 43 3.7709 1 1.1761 1 9

11.00 1 1.3010 13.2 1 65 3.7993 1 1.8195 1 10

11.00 1 1.5682 7.5 1 70 3.8865 0 1.6721 0 12

11.00 1 1.0792 9.6 1 51 3.5051 1 1.9031 0 9

13.00 1 0.7782 5.5 0 60 3.5798 1 1.3979 2 10

14.00 1 1.3979 14.6 1 66 3.7243 1 1.2553 2 10

15.00 1 1.6021 10.6 1 70 3.6902 1 1.4314 0 11

16.00 1 1.3424 9.0 1 48 3.9345 1 2.0000 0 10

16.00 1 1.3222 8.8 1 62 3.6990 1 0.6990 17 10

17.00 1 1.2304 10.0 1 53 3.8808 1 1.4472 4 9

17.00 1 1.5911 11.2 1 68 3.4314 0 1.6128 1 10

18.00 1 1.4472 7.5 1 65 3.5682 0 0.9031 7 8

19.00 1 1.0792 14.4 1 51 3.9191 1 2.0000 6 15

19.00 1 1.2553 7.5 0 60 3.7924 1 1.9294 5 9

24.00 1 1.3010 14.6 1 56 4.0899 1 0.4771 0 9

25.00 1 1.0000 12.4 1 67 3.8195 1 1.6435 0 10

26.00 1 1.2304 11.2 1 49 3.6021 1 2.0000 27 11

32.00 1 1.3222 10.6 1 46 3.6990 1 1.6335 1 9

35.00 1 1.1139 7.0 0 48 3.6532 1 1.1761 4 10

37.00 1 1.6021 11.0 1 63 3.9542 0 1.2041 7 9

41.00 1 1.0000 10.2 1 69 3.4771 1 1.4771 6 10

41.00 1 1.1461 5.0 1 70 3.5185 1 1.3424 0 9

51.00 1 1.5682 7.7 0 74 3.4150 1 1.0414 4 13

52.00 1 1.0000 10.1 1 60 3.8573 1 1.6532 4 10

54.00 1 1.2553 9.0 1 49 3.7243 1 1.6990 2 10

58.00 1 1.2041 12.1 1 42 3.6990 1 1.5798 22 10

66.00 1 1.4472 6.6 1 59 3.7853 1 1.8195 0 9

67.00 1 1.3222 12.8 1 52 3.6435 1 1.0414 1 10

88.00 1 1.1761 10.6 1 47 3.5563 0 1.7559 21 9

89.00 1 1.3222 14.0 1 63 3.6532 1 1.6232 1 9

92.00 1 1.4314 11.0 1 58 4.0755 1 1.4150 4 11

4.00 0 1.9542 10.2 1 59 4.0453 0 0.7782 12 10

4.00 0 1.9243 10.0 1 49 3.9590 0 1.6232 0 13

7.00 0 1.1139 12.4 1 48 3.7993 1 1.8573 0 10

7.00 0 1.5315 10.2 1 81 3.5911 0 1.8808 0 11

8.00 0 1.0792 9.9 1 57 3.8325 1 1.6532 0 8

12.00 0 1.1461 11.6 1 46 3.6435 0 1.1461 0 7

11.00 0 1.6128 14.0 1 60 3.7324 1 1.8451 3 9

12.00 0 1.3979 8.8 1 66 3.8388 1 1.3617 0 9

13.00 0 1.6628 4.9 0 71 3.6435 0 1.7924 0 9

16.00 0 1.1461 13.0 1 55 3.8573 0 0.9031 0 9

19.00 0 1.3222 13.0 1 59 3.7709 1 2.0000 1 10

19.00 0 1.3222 10.8 1 69 3.8808 1 1.5185 0 10

28.00 0 1.2304 7.3 1 82 3.7482 1 1.6721 0 9

41.00 0 1.7559 12.8 1 72 3.7243 1 1.4472 1 9

53.00 0 1.1139 12.0 1 66 3.6128 1 2.0000 1 11

57.00 0 1.2553 12.5 1 66 3.9685 0 1.9542 0 11

77.00 0 1.0792 14.0 1 60 3.6812 0 0.9542 0 12

;

**data** Myeloma2;

set Myeloma;

Contrived= (Time <= **65**);

**run**;

**proc** **format**;

value Contrived **0**='>=65' **1**='<65';

**run**;

**data** Myeloma2;

set Myeloma2;

format Contrived Contrived. ;

**run**;

title 'Table 3 Multivariable Survival Analysis by Firth Correction Cox regression Model';

%***FirthPhreg\_sel*** (dsn= Myeloma2,

event = Time,

censor=Vstatus,

var= LogBUN HGB Contrived,

cVar= Contrived(desc),

inc=**0**,

alpha=**0.09**,

Type3=t,

debug=t,

outpath = &dir.\ ,

filename = Multivariable Firth);

Title;

**Summary Table Example:**

Table 3 Multivariable Survival Analysis by Firth Model

|  | | **Survival Time** | | |
| --- | --- | --- | --- | --- |
|  | | **----------------------------------------** | | |
| **Covariate** | **Level** | **Hazard Ratio (95% CI)** | **HR P-value** | **Type3 P-value** |
| LogBUN |  | 5.53 (1.79-17.57) | **0.003** | **0.003** |
|  | | | | |
| hgb |  | 0.90 (0.79-1.01) | 0.066 | 0.066 |
|  | | | | |
| Contrived | <65 | 15.60 (.-12193.44) | **0.006** | **0.006** |
| >=65 | - | - |
|  | | | | |
| \*  Number of observations in the original data set = 65. Number of observations used = 65. \*\* Backward selection with an alpha level of removal of 0.09 was used. No variables were removed from the model. | | | | |

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**Log of Updates:**