# The SAS MAKESPL Macro 

Ellen Hertzmark, Ruifeng Li, and Donna Spiegelman


#### Abstract

The \%MAKESPL macro is a SAS macro that makes restricted cubic spline variables to be used in procedures. It is incorporated in several of the macros that test for non-linearity, but can also be used on its own to create spline variables for covariates (allowing better control for the covariates usually using up fewer degrees of freedom).


Keywords: SAS, macro, restricted cubic splines, nonlinear relation

## Contents

1. Description
2. Invocation and Details
3. Examples
4. Computational Methods
5. References
6. Credits
7. See Also

## 1: Description

\%MAKESPL is a SAS macro that makes restricted cubic spline variables for a given number of knot points or a list of knots. This macro is useful when you wish to control for confounding by a continuous variable with a possibly non-linear relationship with the outcome.

## 2: Invocation and Details

To call \%MAKESPL, your program must know where to look for it. The most efficient way is to include the following statement (or its equivalent) at the top of your program.
options mautosource sasautos='/usr/local/channing/sasautos';
\%MAKESPL has very few parameters.
DATA The name of data set on which the regression is to be run REQUIRED

SPLVBL The name of the variable to be "splined" REQUIRED

NK The number of knots, if you want \%MAKESPL to place them automatically. The numbers of knots for which automatic knot placement can be done are $3,4,5,6,7,8,9,10,17,21,25$ and 50. See COMPUTATIONAL METHODS for details about knot placement. default is 4

KNOT1 The list of knots if you want to determine them. If you give a value for KNOT1, this takes precedence over any value NK may have.

REFVAL A value of SPLVBL to use as the reference level for procedures that need reference levels (LOGISTIC, log-binomial regression, PHREG) .
The macro prints the values of all the spline variables when SPLVBL = REFVAL. To do this, it adds one observation to the dataset.
default is the minimum value of $\operatorname{SPLVBL}$

NOTE: Sometimes the best way to control for covariates that are originally continuous is to use 3 or 4-knot splines, rather than sets of indicators for categorical levels of the covariates.
For many purposes (such as plotting and estimation), you will need to know the values of the spline variables at a specified value for the covariate. You can find this out by using that specified value as REFVAL.

If you wish to make spline variables for several covariates, you must do them one at a time, using the OUTDAT of one run as the DATA of the next (See Example 1). If you set REFVAL=(value SPLVBL will have in ADJDAT), the macro will print out the values.

NOTE: If the value of REFVAL is outside the range of your data, the macro will give you the following warning message in the . log file.
WARNING: Your REFVAL, <value of REFVAL>, is
lower than all values of the exposure in of the data. The macro will continue, but the graph may look strange. OR
WARNING: Your REFVAL, <value of REFVAL>, is

```
            higher than all values of the exposure in of the data.
            The macro will continue, but the graph may look strange.
                    'The graph may look strange' means that the point for
                which SPLVBL = REFVAL will be included in the plotting points.
                For example, if the range of SPLVBL in the data is 16-40,
                and REFVAL=0, and the predicted value for SPLVBL=0 is a lot
                higher than that for SPLVBL=16, your graph will have a large
                drop from 0 to 16, and all the real information may be squeezed
                into a small part of the graph.
OUTDAT The name of the dataset %MAKESPL will make.
        This dataset includes all the variables in the original
        dataset, plus the newly made spline variables.
        It has the extra observation made for SPLVBL = REFVAL.
        If MAKEPTS = T, it includes the plotting points (See below).
        default=_splstuf
MAKEPTS Whether you want to make 501 plotting points for a graph.
        If MAKEPTS = T, the plotting points in the OUTDAT dataset have
        non-missing values for SPLVBL and COVAR (See below).
        Values the outcome variable in your analysis are missing.
        Because the outcome variable is missing, the plotting points
        will not be used in the estimation routine, but those procedures
        that predict values of the outcome based on the model will
        produce predicted values for the graph.
        The macro makes a variable ({\tt _ine_}) in OUTDAT to distinguish
        the plotting points.
        default is F
COVAR The list of covariates in the model other than SPLVBL.
        This is only required if MAKEPTS=T and there are covariates
        in your model and the vertical axis of your graph will be an
        absolute quantity (predicted probability, value of a continuous
        variable), rather than a relative quantity (relative risk, odds
        ratio).
ADJDAT The name of a data set with one (1) observation containing
        the values of each covariate to be used for plotting,
        IF there are covariates in your model and MAKEPTS=T.
        This is REQUIRED for PROC MIXED and PROC GENMOD based
        procedures, as well as for the PLOTPROB=T option in
        LGTPHCURV8.
```


## 3: Examples

Using a data set from HPFS, we are planning to examine the relationship of a number of risk factors to BMI, cross-sectionally in 1986. We plan to use splines for all the continuous variables.

BMI86 is the individual's BMI in 1986

```
age86 is the individual's age (in years) in 1986
tfat86n is the individual's daily intake of total fat
    in grams per day in 1986
alco86n is the individual's daily intake of alcohol
    in grams per day in 1986
smk86 is the individual's smoking status in 1986
    (0=non-smoker, 1=smoker)
```

Example 1. Making splines for age86 and tfat86n.

To make "spline" variables for age 86 and tfat 86 n , and to print out 3 observations from the output data set each time we ran the macro, we used the following code.

```
title2 'make 4 knot splines for age86';
%makespl(data=alld, splvbl=age86, nk=4, refval=55, outdat=a1);
title2 'first 3 observations of a1';
proc print data=a1 (obs=3);
    var age86 age861 age862 tfat86n alco86n bmi86;
title2 'make 5 knot splines for tfat86n';
%makespl(data=a1, splvbl=tfat86n, nk=5, refval=70, outdat=a2);
title2 'first 3 observations of a2';
proc print data=a2 (obs=3);
    var age86 age861 age862 tfat86n tfat86n1 tfat86n2 tfat86n3
    alco86n bmi86;
run;
```

By using the output data set (OUTDAT) from the first run of \%MAKESPL as the input data set (DATA) for the second run of \%MAKESPL, the output data set of the second run (a2) has the spline variables for age86 and for tfat86n.

Since we are not planning to do the analysis before running we left MAKEPTS $=\mathrm{F}$ (the default) both times.

Since NK for age 86 was 4, the "spline" variables for age 86 are named age861 and age 862. Since NK for tfat86n was 5, the "spline" variables for tfat86n are named tfat86n1, tfat $86 n 2$, and tfat86n3. In general the names will be variable name 1 ...variable name(nk-2), where NK is the number of knots, either given to the macro or counted from a list given in KNOT1.

The results of the above bit of program are shown below.
First the macro lists the knot locations.
Because we gave the value 55 for REFVAL in the first call to \%MAKESPL and 70 for REFVAL in the second call to \%MAKESPL, we get printouts of the values of the "spline" variables at the reference values. If we had not given a value for REFVAL, the macro would have used the
default value (the minimum value of age 86), and all spline variables would have had value 0 (because the first knot is greater than the minimum).
We will use these in the ADJDAT86 data set (see Example 2).


```
/udd/stleh/helpme/pkb/splex.sas 4
make 4 knot splines for age86 15:17 Wednesday, July 24, 2002
Knots for age86
    40465467
```



```
/udd/stleh/helpme/pkb/splex.sas 5
make 4 knot splines for age86 15:17 Wednesday, July 24, 2002
values of spline variables when age86 is 55
    OBS AGE86 AGE861 AGE862
11766 55 4.62678 0.99778
```



```
/udd/stleh/helpme/pkb/splex.sas
6
first 3 observations of a1 15:17 Wednesday, July 24, 2002
\begin{tabular}{rrrrrrr} 
OBS & AGE86 & AGE861 & AGE862 & TFAT86N & ALCO86N & BMI86 \\
& & & & & & \\
1 & 69 & 23.8519 & 9.2181 & 41.2 & 0.0 & 25.1 \\
2 & 73 & 30.0741 & 11.9835 & 34.1 & 39.7 & 24.3 \\
3 & 72 & 28.5185 & 11.2922 & 79.2 & 0.0 & 26.3
\end{tabular}
```


## 

```
/udd/stleh/helpme/pkb/splex.sas
```

/udd/stleh/helpme/pkb/splex.sas
make 5 knot splines for tfat86n 15:17 Wednesday, July 24, 2002
make 5 knot splines for tfat86n 15:17 Wednesday, July 24, 2002
Knots for tfat86n
Knots for tfat86n
35.7 53.8 67.5 82.7 110.6

```
    35.7 53.8 67.5 82.7 110.6
```



```
/udd/stleh/helpme/pkb/splex.sas 8
make 5 knot splines for tfat86n 15:17 Wednesday, July 24, 2002
values of spline variables when tfat86n is 70
    OBS TFAT86N TFAT86N1 TFAT86N2 TFAT86N3
11767 70 7.19314 0.75785 .0027852
```

```
/udd/stleh/helpme/pkb/splex.sas
first 3 observations of a2 15:17 Wednesday, July 24, 2002
\begin{tabular}{cccccccccc} 
& & & & & T & T & T & \\
& & & & T & F & F & F & A & \\
& & A & A & F & A & A & A & L & \\
& A & G & G & A & T & T & T & C & B \\
& G & E & E & T & 8 & 8 & 8 & O & M \\
O & E & 8 & 8 & 8 & 6 & 6 & 6 & 8 & I \\
B & 8 & 6 & 6 & 6 & N & N & N & 6 & 8 \\
S & 6 & 1 & 2 & N & 1 & 2 & 3 & N & 6
\end{tabular}
    1 69 23.8519 9.2181 41.2 0.0297 0.00000 0.00000 0.0 25.1
    2 73 30.0741 11.9835 34.1 0.0000 0.00000 0.00000 39.7 24.3
    3 72 28.5185 11.2922 79.2 14.6725 2.92104 0.28549 0.0 26.3
```

Example 2. Making the data set with plotting points for ALCO86N
We begin where Example 1 left off.

```
/* make data set with one observation to give values of covariates
for plotting points.
We got these values from the MAKESPL above,
because we gave values for REFVAL */
data adjdat86;
age86=55; age861=4.626778; age862=.9978; tfat86n=70;
tfat86n1=7.19314; tfat86n2=.75785; tfat86n3=.002852; smk86=0;
run;
title2 'make 3 knot splines for ALCO86N. make plotting points';
%makespl(data=a2, splvbl=alco86n, nk=3, makepts=T, refval=0,
covar=age86 age861 age862
tfat86n tfat86n1 tfat86n2 tfat86n3 smk86,
adjdat=adjdat86, outdat=a3);
title2 'first 3 observations in a3 ';
proc print data=a3 (obs=3);
var age86 age861 age862 tfat86n tfat86n1 tfat86n2 tfat86n3
alco86n alco86n1 bmi86 smk86;
```

```
run;
title2 'first 5 plotting points';
data pltpts; set a3; where ine_ eq 1;
proc print data=pltpts (obs=5);
var age86 age861 age862 tfat86n tfat86n1 tfat86n2 tfat86n3
alco86n alco86n1 bmi86 smk86;
run;
```

The variable _ine_ is an indicator for being a plotting point (for the latest run of \%MAKESPL). The results of this bit of code are below.

```
[ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [
/udd/stleh/helpme/pkb/splex.sas 10
first 3 observations of a3 15:17 Wednesday, July 24, 2002
Knots for alco86n
    0 6 35.1
```


/udd/stleh/helpme/pkb/splex.sas
11
first 3 observations of a3 15:17 Wednesday, July 24, 2002
values of spline variables when alco86n is 0
OBS ALCO86N ALCO86N1

| 11768 | 0 | 0 |
| :--- | :--- | :--- |
| 12269 | 0 | 0 |

[ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [
/udd/stleh/helpme/pkb/splex.sas 12
first 3 observations of a3
15:17 Wednesday, July 24, 2002
OBS AGE86 AGE861 AGE862 TFAT86N TFAT86N1 TFAT86N2

| 1 | 69 | 23.8519 | 9.2181 | 41.2 | 0.0297 | 0.00000 |
| ---: | ---: | ---: | ---: | ---: | ---: | ---: |
| 2 | 73 | 30.0741 | 11.9835 | 34.1 | 0.0000 | 0.00000 |
| 3 | 72 | 28.5185 | 11.2922 | 79.2 | 14.6725 | 2.92104 |

    OBS TFAT86N3 ALCO86N ALCO86N1 BMI86 SMK86
        \(\begin{array}{lllll}1 & 0.00000 & 0.0 & 0.0000 & 25.1\end{array}\)
        \(\begin{array}{llllll}2 & 0.00000 & 39.7 & 13.3333 & 24.3 & 0\end{array}\)
        \(\begin{array}{llllll}3 & 0.28549 & 0.0 & 0.0000 & 26.3 & 0\end{array}\)
    [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [
/udd/stleh/helpme/pk.b/splex.sas


## 

Note that in the plotting points, bmi 86, which is neither SPLVBL nor in the COVAR list, is missing. Also, values for the age 86 , tfat86n, and smk86 variables are all the same (= the plotting levels from ADJDAT86).

Example 3. Specifying the knots for ALCO86N in advance
Below we show the code and the results from specifying the knots for ALCO86N at 0,2 , and 35 , instead of the automatic locations of 0,6 , and 35.1 .

```
title2 'make spline variables for ALC86 (=ALCO86N) with knots given';
%makespl(data=a3, splvbl=alc86, knot1=0 2 35, makepts=T,
covar=age86 age861 age862 tfat86n tfat86n1 tfat86n2 tfat86n2 smk86,
adjdat=adjdat86, refval=0, outdat=a4);
title2 'first 6 observations of a4';
proc print data=a4 (obs=6);
var age86 age861 age862 tfat86n tfat86n1 tfat86n2 tfat86n3
alco86n alco86n1 alc86 alc861 bmi86 smk86;
run;
```



```
/udd/stleh/helpme/pkb/splex.sas 14
make spline variables for ALC86 (=ALCO86N) with knots given
    15:17 Wednesday, July 24, 2002
Knots for alc86
    0 35
```

```
/udd/stleh/helpme/pkb/splex.sas 15
make spline variables for ALC86 (=ALCO86N) with knots given
    15:17 Wednesday, July 24, 2002
values of spline variables when alc86 is 0
    OBS ALC86 ALC861
12270 0 0
12771 0 0
```



```
/udd/stleh/helpme/pkb/splex.sas 16
first 6 observations of a4
                                    15:17 Wednesday, July 24, 2002
    OBS age86 age861 age862 TFAT86N TFAT86N1 TFAT86N2 TFAT86N3
\begin{tabular}{rrrrrrrr}
1 & 69 & 23.8519 & 9.2181 & 41.2 & 0.0297 & 0.0000 & 0.00000 \\
2 & 73 & 30.0741 & 11.9835 & 34.1 & 0.0000 & 0.0000 & 0.00000 \\
3 & 72 & 28.5185 & 11.2922 & 79.2 & 14.6725 & 2.9210 & 0.28549 \\
4 & 67 & 20.7407 & 7.8354 & 69.9 & 7.1304 & 0.7439 & 0.00246 \\
5 & 69 & 23.8519 & 9.2181 & 83.3 & 19.2245 & 4.5761 & 0.70303 \\
6 & 66 & 19.1867 & 7.1449 & 96.6 & 38.9762 & 13.0009 & 3.65301
\end{tabular}
OBS ALCO86N ALCO86N1 ALC86 ALC861 BMI86 SMK86
\begin{tabular}{rrrrrrr}
1 & 0.0 & 0.0000 & 0.0 & 0.00000 & 25.1 & 0 \\
2 & 39.7 & 13.3333 & 39.7 & 4.69143 & 24.3 & 0 \\
3 & 0.0 & 0.0000 & 0.0 & 0.00000 & 26.3 & 0 \\
4 & 16.6 & 2.5468 & 16.6 & 1.03963 & 22.6 & 0 \\
5 & 11.2 & 1.0027 & 11.2 & 0.47269 & 28.4 &. \\
6 & 2.7 & 0.0160 & 2.7 & 0.01577 & 21.9 & 0
\end{tabular}
```


## [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [

In this example, we printed out the values of the "spline" variables we got from the previous run (with automatic knot placement), as well as the values of the "spline" variables we got from this call to \%MAKESPL. Because the knots are in different locations, the values of the "spline" variables are different unless the value of $\mathrm{ALCO} 6 \mathrm{~N}=\mathrm{ALC} 86$ is 0 .

Example 4. Automatic knot placement does not yield distinct knots
Since alcohol consumption is skewed toward 0 , requiring a large number of knots will lead to at least two of the knots having value 0 . This causes an ERROR message.

```
title2 'try to make 8-knot splines for ALCO86N';
%makespl(data=a4, splvbl=alc86, nk=8, makepts=T, refval=0,
covar=age86 age861 age862 tfat86n tfat86n1 tfat86n2 tfat86n2 smk86,
adjdat=adjdat86, outdat=a5);
```



```
/udd/stleh/helpme/pkb/splex.sas 17
try to make 8-knot splines for ALCO86N
    15:17 Wednesday, July 24, 2002
Knots for alc86
    0 0 1.9 4.6 8.7 14 23.4 69.8
    "
```


## [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [

```
/udd/stleh/helpme/pkb/splex.sas
```

/udd/stleh/helpme/pkb/splex.sas
1 8
1 8
try to make 8-knot splines for ALCO86N
15:17 Wednesday, July 24, 2002
ERROR in macro run: The spline-making procedure did not generate
8 distinct knot points.
You will either have to change the number of knot points
or supply values for the knots, i.e. KNOT1=
The macro will terminate.

```


NOTE: In the women's cohorts, it may be impossible to use automatic placement for 4 knot splines for alcohol intake variables.

\section*{4: Computational Methods}

\section*{1. Automatic Knot Placement}
```

nk percentile locations of the knots
5 50 95
5 35 65 95
5 27.5 50 72.5 95
5 23 41 59 77 95
2.5 18.3 34.2 50 65.8 81.7 97.5
1 15 29 43 57 71 85 99
2 14 26 38 50 62 74 86 98
2 12.7 23.3 34 44.7 55.3 68 76.7 87.3 98
2
1 4 9 14 19 24 29 34 39 44 49 54 59 64 69 74 79 84 89 94 99
2 6 10 14 18 22 26 30 34 38 42 46 50 54 58 62 66
70 74 78 82 86 90 94 98
50}1
37}3944143454749 51 53 55 57 59 61 63 65 67
69 71 73 75 77 79 81 83 85 87 899 91 93 95 97 99

```

\section*{2 Computation of the spline variables:}

Let \(\mathrm{t}_{\mathrm{j}}\) be the jth knot point.
Let \(k d=\left(t_{n k}-t_{1}\right)^{2 / 3}\), where \(k d\) is a normalizing parameter to get the spline variables back into the original units.

For a level of the exposure x , xj , the value of the jth spline variable ( j runs from 1 to NK-2) is given by
\[
\begin{gathered}
x_{j}=\max \left(\left(x-t_{j}\right) / k d, 0\right)^{3} \\
+\left(t_{n k-1}-t_{j}\right) * \max \left(\left(x-t_{n k}\right) / k d, 0\right)^{3} \\
\left.-\left(t_{n k}-t_{j}\right) * \max \left(\left(x-t_{n k-1}\right) / k d, 0\right)^{3}\right) /\left(t_{n k}-t_{n k-1}\right)
\end{gathered}
\]

For \(\mathrm{x}<\mathrm{t}_{\mathrm{j}}\) the value of the jth spline variable is 0 (as are the 'higher' spline variables) (because all the 'max' values are 0 , since \(\mathrm{x}<\mathrm{t}_{\mathrm{j}}<\mathrm{t}_{\mathrm{nk}-1}<\mathrm{t}_{\mathrm{nk}}\). As x gets larger, it has more and more nonzero spline variables.

As an example, we show the values of the 3 "spline" variables for the 5 knot splines of tfat86n. The graph below was made using the 'plotting points' using the following code.
```

%makespl( data=alld, splvbl=tfat86n, nk=5, makepts=T, outdat=a99);
data inest; set a99;
if _ine_ eq 1;
run;

```

This code uses the automatic _ine_ variable to select the 'plotting points.'


The reference lines are at the knot locations.
In fact, tfat 86 n 1 becomes nonzero at the first knot, tfat 86 n 2 becomes nonzero at the second knot, and tfat 86 n 3 becomes nonzero at the third knot. Because of the large range of the vertical axis, this is not visible on the graph.

\section*{5: References}
```

ovindarajulu U.S., Spiegelman D., Thurston S.W., Ganguli B.,
Eisen E.A.: "Comparing smoothing techniques in Cox models for
exposure-response relationships". Statistics in Medicine, 2007;
26:3735-3752.
Govindarajulu U.Malloy, E.J., Ganguli, B., Spiegelman, D, Eisen, E.A.:
A comparison of fitted non-linear exposure-response relationships
in Cox models using smoothing methods through simulations.
In preparation, 2007.

```
```

Smith, Patricia L.: Splines as a useful and convenient
statistical tool. The American Statistician 33(2): 57-, 1979.
Harrell, Frank E, Jr., Lee, Kerry L., Pollock, Barbara G.:
Regression models in clinical studies: determining relationships
between predictors and response. JNCI 80: 1198-1202, 1988.
Durrleman, Sylvain, and Simon, Richard: Flexible regression
models with cubic splines. Statistics in Medicine
8: 551-561, 1989.
Devlin TF, Weeks BJ (1986): Spline functions for logistic
regression modeling. Proc Eleventh Annual SAS Users Group
International. Cary NC: SAS Institute, Inc., pp. 646-51.
Stone CJ, Koo CY (1985): Additive splines in statistics.
Proc Stat Comp Sect Am Statist Assoc, pp. 45-8.
Stone CJ (1986): Comment, pp. 312-314, to paper by
Hastie T. and Tibshirani R. (1986): Generalized additive
models. Statist Sciences 1:297-318.

```

\section*{6: Credits}

Written by Ellen Hertzmark and Donna Spiegelman for the Channing Laboratory. Based on a macro by Frank Harrell. Questions can be directed to Ellen Hertzmark, stleh@channing.harvard.edu, (617) 432-4957.

\section*{7: See Also}

Channing SAS macro \%LGTPHCURV9```

