Stata Technical Bulletin

A publication to promote communication among Stata users

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The Stata Technical Bulletin (ISSN 1097-8879) is published six times per year by Stata Corporation. Stata is a registered trademark of Stata Corporation.

Contents of this issue

page

an69.	STB-43-STB-48 available in bound format	2
dm45.1.	Changing string variables to numeric: update	2
dm65.	A program for saving a model fit as a dataset	2
dm66.	Recoding variables using grouped values	6
dm67.	Numbers of missing and present values	7
gr34.2.	Drawing Venn diagrams	8
gr36.	An extension of for, useful for graphics commands	8
gr37.	Cumulative distribution function plots	10
sbe27.	Assessing confounding effects in epidemiological studies	12
sbe28.	Meta-analysis of p-values	15
sg64.1.	Update to pwcorrs	17
sg81.1.	Multivariable fractional polynomials: update	17
sg97.1.	Revision of outreg	23
sg107.1.	Generalized Lorenz curves and related graphs	23
sg111.	A modified likelihood-ratio test command	24
sg112.	Nonlinear regression models involving power or exponential functions of covariates	25
ssa13.	Analysis of multiple failure-time data with Stata	30
zz9.	Cumulative index for STB-43-STB-48	40

an69	STB-43–STB-48 available in bound format
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Patricia Branton, Stata Corporation, stata@stata.com

The eighth year of the *Stata Technical Bulletin* (issues 43–48) has been reprinted in a bound book called *The Stata Technical Bulletin Reprints, Volume 8*. The volume of reprints is available from StataCorp for \$25, plus shipping. Authors of inserts in STB-43–STB-48 will automatically receive the book at no charge and need not order.

This book of reprints includes everything that appeared in issues 43-48 of the STB. As a consequence, you do not need to purchase the reprints if you saved your STBs. However, many subscribers find the reprints useful since they are bound in a convenient volume. Our primary reason for reprinting the STB, though, is to make it easier and cheaper for new users to obtain back issues. For those not purchasing the *Reprints*, note that *zz9* in this issue provides a cumulative index for the eighth year of the original STBs.

dm45.1	Changing string variables to numeric: update
	Nicholas J. Cox, University of Durham, UK, n.j.cox@durham.ac.uk

Syntax

destring [varlist] [, <u>noc</u>onvert <u>noe</u>ncode <u>f</u>loat]

Remarks

destring was published in STB-37. Please see Cox and Gould (1997) for a full explanation and discussion. It is here translated into the idioms of Stata 6.0. The main substantive change is that because value labels may now be as long as 80 characters, string variables of any length, from str1 to str80, may be encoded to numeric variables with string labels.

Reference

Cox, N. J. and W. Gould. 1997. dm45: Changing string variables to numeric. Stata Technical Bulletin 37: 4–6. Reprinted in Stata Technical Bulletin Reprints, vol. 7, pp. 34–37.

dm65	A program for saving a model fit as a dataset
	Roger Newson, Imperial College School of Medicine, London, UK, r.newson@ic.ac.ul

The command parmest is designed to save a model fit in a data set, either in memory, or on disk, or both. It was inspired by the example of collapse. It takes, as input, the parameter estimates of the most recently fitted model, and their covariance matrix. It creates, as output, a new dataset, with one observation per parameter, and variables corresponding to equation names (if present), parameter names, estimates, standard errors, z or t test statistics, p-values and confidence limits. This output dataset may be saved to a disk file, or remain in memory (overwriting the pre-existing dataset), or both.

Typically, parmest is used with graph to produce confidence interval plots. It is also possible to sort the output dataset by *p*-value, in order to carry out closed test procedures, like those of Holm, Hommel, or Holland and Copenhaver, summarized in Wright (1992).

Syntax

parmest [, dof(#) label eform level(#) fast saving(filename[, replace]) norestore]

Options

- dof (#) specifies the degrees of freedom for t-distribution-based confidence limits. If dof is zero, then confidence limits are calculated using the standard normal distribution. If dof is absent, it is set to a default according to the last estimation results.
- label indicates that a variable named *label* is to be generated in the new dataset, containing the variable labels of variables corresponding to the parameter names, if such variables can be found in the existing dataset.
- eform indicates that the estimates and confidence limits are to be exponentiated, and the standard errors multiplied by the exponentiated estimates.
- level(#) specifies the confidence level, in percent, for confidence limits. The default is level(95) or as set by set level. (See [U] Estimation and post-estimation commands.)

- fast specifies that parmest not go to extra work so that it can restore the original data should the user press Break. fast is intended for use by programmers.
- saving(filename[,replace]) saves the output dataset in a file. If replace is specified, and a file of name filename already
 exists, then the old file is overwritten.
- norestore specifies whether or not the pre-existing dataset is restored at the end of execution. This option is automatically set to norestore if fast is specified or saving (*filename*) is absent, otherwise it defaults to restoring the pre-existing dataset.

Remarks

parmest creates a new dataset with one observation per parameter and data on the most recent model fit. There are two character variables, eq and parm, containing equation and parameter names, respectively. The numeric variables are estimate, stderr, z (or t), p, minxx and maxxx, where xx is the value of the level option. These variables contain parameter estimates, standard errors, z test (or t test) statistics, p-values, and confidence limits, respectively. The p-values test the hypothesis that the appropriate parameter is zero, or one if eform is specified.

Example

This example uses the Stata example dataset auto.dta, with the added variable manuf, containing the first word of make, and denoting manufacturer. (See [U] 26.10 Obtaining robust variance estimates for an example of the use of this variable.) We want to derive confidence intervals for the average fuel efficiency (in miles per gallon) for each manufacturer, using a homoscedastic regression model. (Some manufacturers are represented by only one model in the dataset, so their specific variances cannot be estimated.) We then want to plot the confidence intervals by manufacturer.

We proceed as follows. First we tabulate manuf, generating the dummy variables for the regression analysis:

. tabulate ma	nui,missing	gene (manu)	
Manufacturer	Freq.	Percent	Cum.
++ AMC	3	4.05	4.05
Audi	2	2.70	6.76
BMW	1	1.35	8.11
Buick	7	9.46	17.57
Cad.	3	4.05	21.62
Chev.	6	8.11	29.73
Datsun	4	5.41	35.14
Dodge	4	5.41	40.54
Fiat	1	1.35	41.89
Ford	2	2.70	44.59
Honda	2	2.70	47.30
Linc.	3	4.05	51.35
Mazda	1	1.35	52.70
Merc.	6	8.11	60.81
Olds	7	9.46	70.27
Peugeot	1	1.35	71.62
Plym.	5	6.76	78.38
Pont.	6	8.11	86.49
Renault	1	1.35	87.84
Subaru	1	1.35	89.19
Toyota	3	4.05	93.24
VW	4	5.41	98.65
Volvo	1	1.35	100.00
Total	74	100.00	

. tabulate manuf,missing gene(manu)

We then carry out a regression analysis of mpg with respect to the dummy variables:

. regress mpg manu1-manu23, noconst

Source	1	SS	df	MS	Number of obs =	=	74
	+-				F(23, 51)=	=	70.51
Model		34910.1286	23	1517.83168	Prob > F =	=	0.0000
Residual	1	1097.87143	51	21.5268908	R-squared =	=	0.9695
	+-				Adj R-squared =	=	0.9558
Total		36008.00	74	486.594595	Root MSE	=	4.6397

STB-49	9
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mpg	Coef.	Std. Err.	t	P> t	[95% Conf.	Interval]
manu1	20.33333	2.678737	7.591	0.000	14.95555	25.71112
manu2	20	3.280769	6.096	0.000	13.41358	26.58642
manu3	25	4.639708	5.388	0.000	15.6854	34.3146
manu4	19.14286	1.753645	10.916	0.000	15.62227	22.66345
manu5	16.33333	2.678737	6.097	0.000	10.95555	21.71112
manu6	22	1.894153	11.615	0.000	18.19733	25.80267
manu7	25.75	2.319854	11.100	0.000	21.0927	30.4073
manu8	20.25	2.319854	8.729	0.000	15.5927	24.9073
manu9	21	4.639708	4.526	0.000	11.6854	30.3146
manu10	24.5	3.280769	7.468	0.000	17.91358	31.08642
manu11	26.5	3.280769	8.077	0.000	19.91358	33.08642
manu12	12.66667	2.678737	4.729	0.000	7.288878	18.04445
manu13	30	4.639708	6.466	0.000	20.6854	39.3146
manu14	17.16667	1.894153	9.063	0.000	13.364	20.96934
manu15	19.42857	1.753645	11.079	0.000	15.90798	22.94916
manu16	14	4.639708	3.017	0.004	4.685398	23.3146
manu17	26.2	2.074941	12.627	0.000	22.03438	30.36562
manu18	19.5	1.894153	10.295	0.000	15.69733	23.30267
manu19	26	4.639708	5.604	0.000	16.6854	35.3146
manu20	35	4.639708	7.544	0.000	25.6854	44.3146
manu21	22.33333	2.678737	8.337	0.000	16.95555	27.71112
manu22	28.5	2.319854	12.285	0.000	23.8427	33.1573
manu23	17	4.639708	3.664	0.001	7.685398	26.3146

We then use parmest to save the parameter estimates, and their confidence limits, to the new dataset.

. parm	nest,lab			
. desc	cribe			
Contai	ins data			
obs:	:	23		
vars:	:	8		
size:	:	1,656 (82.7% of m	emory free)	
1.	parm	str6 %9s		Parameter name
2.	label	str14 %14s		Parameter label
3.	estimate	double %10.0g		Parameter estimate
4.	stderr	double %10.0g		SE of parameter estimate
5.	t	double %10.0g		t-test statistic
6.	р	double %10.0g		P-value
7.	min95	double %10.0g		Lower 95% confidence limit
8.	max95	double %10.0g		Upper 95% confidence limit
Sorter				
NOTCEC	Iote: dat	a has changed sin	co last save	<u>م</u>
		a has changed sin	ce rast save	
. list	5 parm lab	el estimate stder	r	
	\mathtt{parm}	label	estimate	stderr
1.	manu1	manuf==AMC	20.333333	2.6787367
2.	manu2	manuf==Audi	20	3.280769
З.	manu3	manuf==BMW	25	4.639708
4.	manu4	manuf==Buick	19.142857	1.7536448
5.	manu5	manuf==Cad.	16.333333	2.6787367
6.	manu6	manuf == Chev.	22	1.8941529
7.	manu7	manuf==Datsun	25.75	2.319854
8.	manu8	manuf==Dodge	20.25	2.319854
9.	manu9	manuf==Fiat	21	4.639708
10.	manu10	manuf==Ford	24.5	3.280769
11.	manu11	manuf==Honda	26.5	3.280769
12.	manu12	manuf==Linc.	12.666667	2.6787367
13.	manu13	manuf==Mazda	30	4.639708
14.	manu14	manuf==Merc.	17.166667	1.8941529
15.	manu15	manuf==01ds	19.428571	1.7536448
16.	manu16	manuf==Peugeot	14	4.639708
17.	manu17	manuf==Plym.	26.2	2.0749405
18.	manu18	manuf==Pont.	19.5	1.8941529
19.	manu19	manuf==Renault	26	4.639708
20.	manu20	manuf==Subaru	35	4.639708
21.	manu21	manuf==Toyota	22.333333	2.6787367
22.	manu22	manuf==VW	28.5	2.319854
23.	manu23	manuf==Volvo	17	4.639708

. list parm estimate min95 max95	5 t	p
----------------------------------	-----	---

	parm	estimate	min95	max95	t	р
1.	manu1	20.333333	14.955545	25.711122	7.5906428	6.372e-10
2.	manu2	20	13.413581	26.586419	6.0961317	1.450e-07
3.	manu3	25	15.685398	34.314602	5.3882701	1.830e-06
4.	manu4	19.142857	15.622268	22.663446	10.91604	5.972e-15
5.	manu5	16.333333	10.955545	21.711122	6.0974016	1.443e-07
6.	manu6	22	18.19733	25.80267	11.614691	6.151e-16
7.	manu7	25.75	21.092699	30.407301	11.099836	3.265e-15
8.	manu8	20.25	15.592699	24.907301	8.7289975	1.074e-11
9.	manu9	21	11.685398	30.314602	4.5261469	.00003625
10.	manu10	24.5	17.913581	31.086419	7.4677613	9.947e-10
11.	manu11	26.5	19.913581	33.086419	8.0773745	1.100e-10
12.	manu12	12.666667	7.2888785	18.044455	4.7285971	.00001823
13.	manu13	30	20.685398	39.314602	6.4659241	3.796e-08
14.	manu14	17.166667	13.363996	20.969337	9.0629784	3.306e-12
15.	manu15	19.428571	15.907983	22.94916	11.078966	3.496e-15
16.	manu16	14	4.6853976	23.314602	3.0174312	.00397119
17.	manu17	26.2	22.034383	30.365617	12.626868	2.553e-17
18.	manu18	19.5	15.69733	23.30267	10.29484	4.745e-14
19.	manu19	26	16.685398	35.314602	5.6038009	8.504e-07
20.	manu20	35	25.685398	44.314602	7.5435781	7.557e-10
21.	manu21	22.333333	16.955545	27.711122	8.3372634	4.332e-11
22.	manu22	28.5	23.842699	33.157301	12.285256	7.363e-17
23.	manu23	17	7.6853976	26.314602	3.6640236	.00059118

We then augment this new dataset with two new variables, the character variable manufb and the numeric variable manufn, derived from the variable labels stored in label, and representing the first two letters of the manufacturer's name. Finally, we use manufn to create a confidence interval plot for mean fuel efficiencies by manufacturer:

```
. gene str2 manufb=substr(label,length("manuf==")+1,2)
. encode manufb,gene(manufn)
. set textsize 100
. graph estimate min95 max95 manufn,c(.II) s(0..)
>
  xscale(0.5,23.5)
>
  xlabel(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23)
  yscale(0,45) ylabel(0,5,10,15,20,25,30,35,40,45)
>
>
  t1title(" ") t2title(" ")
 b2title("Manufacturer") l2title("Mileage (miles per gallon)")
>
>
  saving(fig1.gph,replace);
```

The graph generated by this program is given as Figure 1.



Figure 1. Confidence interval plot for mean fuel efficiencies by manufacturer.

Acknowledgments

I would like to thank Nick Cox of Durham University, UK, Jonah B. Gelbach at the University of Maryland at College Park, and Phil Ryan at the Department of Public Health, University of Adelaide, Australia for giving many helpful suggestions for improvements on previous versions posted to Statalist.

Reference

Wright, S. P. 1992. Adjusted p-values for simultaneous inference. Biometrics 48: 1005-1013.

dm66 Recoding variables using grouped values	dm66	Recoding variables using grouped values
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David Clayton, MRC Biostatistical Research Unit, Cambridge, david.clayton@mrc-bsu.cam.ac.uk Michael Hills (retired), mhills@regress.demon.co.uk

This insert describes a new option in egen which creates a new categorical variable from a metric variable. The categorical variable is coded with either the left-hand ends of the grouping intervals specified, or the integer codes 0, 1, 2, etc. The integer codes can be labeled with the left-hand ends of the intervals. If no intervals are specified, the command creates k groups for which the frequency of observations are approximately equal. Missing values are ignored when counting the frequencies.

Syntax

```
egen newvar = cut(varname), { <u>br</u>eaks(#,#,...,#) | group(#) } [ <u>ic</u>odes <u>lab</u>el ]
```

Options

- breaks(#,#,...,#) supplies the breaks for the groups, in ascending order. The list of break points may be simply a list of numbers separated by commas, but can also include the syntax a[b]c, meaning from a to c in steps of size b. If no breaks are specified, the command expects the option group().
- group(#) specifies the number of equal frequency grouping intervals to be used in the absence of breaks. Specifying this option automatically invokes icodes.

icodes requests that the codes 0, 1, 2, etc. be used in place of the left-hand ends of the intervals.

label requests that the integer coded values of the grouped variable be labeled with the left-hand ends of the grouping intervals. Specifying this option automatically invokes icodes.

Example

Using the variable length from the auto data, the commands

```
. egen lgrp = cut(length), breaks(140,180,200,220,240)
. tab lgrp
```

produce the output

lgrp	Freq.	Percent	Cum.
+ 140	31	41.89	41.89
180	16	21.62	63.51
200	20	27.03	90.54
220	7	9.46	100.00
Total	74	100.00	

as will the command

. egen lgrp = cut(length), breaks(140, 180[20]240)

Values outside the range 140-240 are coded as missing. The command

. egen lgrp = cut(length), breaks(140,180[20]240) icodes

will produce a variable coded 0, 1, 2, 3, and adding the option label will label the integer coded values of the grouped variable with the labels 140-, 180-, 200-, 220-. Finally the commands

. egen lgrp = cut(length), group(5) label
. tab lgrp

will produce the output

lgrp	Freq.	Percent	Cum.
142-	12	16.22	16.22
165-	16	21.62	37.84
179-	14	18.92	56.76
198-	15	20.27	77.03
206-	17	22.97	100.00
Total	74	100.00	

The algorithm for producing equal frequency groups is to first use the Stata command pctile to calculate the quantiles, and then to use these together with the extreme values of the variable being cut, as breaks. The result is groups of approximately equal frequency with the additional property that duplicate observations must all lie in the same group.

Discussion

Some of these results could be obtained using the Stata commands summarize, pctile and xtile. For example,

```
. summarize length
. pctile pct = length, nq(5)
. xtile lgrp = length, cut(pct)
```

is equivalent to

. egen lgrp = cut(length), group(5)

but the cut option in egen puts everything in the same table. Theoretically, xtile could be used to reproduce the results from

. egen lgrp = cut(length), breaks(140,180,200,220,240)

but in practice this would be cumbersome, because the breaks need to be in a variable. The Stata function recode() is also a candidate, but now the grouped categorical variable is coded with the right-hand ends. In spite of overlap with these existing commands, it seems to us that there is room for a new one which combines all the common requirements when categorizing a metric variable in a simple way.

dm67	Numbers of missing and present values
------	---------------------------------------

Nicholas J. Cox, University of Durham, UK, n.j.cox@durham.ac.uk

Syntax

```
nmissing [varlist] [if exp] [in range] [, min(#)]
npresent [varlist] [if exp] [in range] [, min(#)]
```

Description

nmissing lists the number of missing values in each variable in *varlist*. Missing means . for numeric variables and the empty string "" for string variables.

npresent lists the number of present (nonmissing) values in each variable in varlist.

Options

min(#) specifies that only numbers at least # should be listed. The default is one.

Remarks

Suppose you want a concise report on the numbers of missing values in a large dataset. You are interested in string variables as well as numeric variables. Existing Stata commands do not serve this need. summarize is biased towards numeric variables and reports all string variables as having 0 observations, meaning 0 observations that can be treated as numeric. inspect has the same bias, and in any case has no concise mode. codebook comes nearer, in that strings are treated as strings and not as failed numeric variables, but it again has no concise mode.

nmissing is an attempt to fill this gap. When called with no arguments it reports on the whole dataset, including both numeric and string variables. If a *varlist* is specified, or the minimum number of values to be reported is specified by the min() option, then the focus is restricted accordingly.

npresent is the complementary command that reports on present (nonmissing) values. nmissing and npresent are written for Stata 6.0.

The user-written command pattern (Goldstein 1996a, 1996b) may also be useful in this connection. It reports, as the name implies, on the pattern of missing data for one or more variables.

Examples

With the familiar auto dataset,

	. nmissing	
yields		
	rep78	5
while		
	. nmissing if	foreign
yields		
	rep78	1

References

Goldstein, R. 1996a. sed10: Patterns of missing data. *Stata Technical Bulletin* 32: 12–13. Reprinted in *Stata Technical Bulletin Reprints*, vol. 6, p. 115. ——. 1996b. sed10.1: Update to pattern. *Stata Technical Bulletin* 33: 2. Reprinted in *Stata Technical Bulletin Reprints*, vol. 6, pp. 115–116.

gr34.2	Drawing Venn diagrams

Jens M. Lauritsen, County of Fyn, Denmark, jm.lauritsen@dadlnet.dk

The Venn diagram routine has been updated to allow more than 32,767 observations. An error in the previous version found by Steven Stillman has been corrected. The error made the contents of a generated variable faulty, in particular with missing data. The counts in the actual Venn Diagram Graph have been correct in previous versions.

References

Lauritsen, J. M. 1999a. gr34: Drawing Venn diagrams. Stata Technical Bulletin 47: 3–8.
—. 1999b. gr34.1: Drawing Venn diagrams. Stata Technical Bulletin 48: 2.

gr36	An extension of for, useful for graphics commands

Jeroen Weesie, Utrecht University, Netherlands, J.Weesie@fss.uu.nl

Arguably, one of the most useful and powerful features of Stata is the for command that allows the simple programming of the repetition of commands with somewhat different arguments. However, for graphics commands I find the for command somewhat inconvenient; rather than inspecting the graphs one at a time, I want to look at a single *combined plot* to facilitate comparison of the plots. To make this easier, I wrote forgraph which is actually just a slight modification of the for command. To look at histograms for a number of variables from the Stata automobile data, one can issue the command

forgraph price-hdroom: graph @, hist xlab ylab

which gives Figure 1.



Figure 1. Using forgraph to obtain four histograms.

forgraph works with other graphics commands as well. To obtain a plot for kernel density estimates of these variables one can use the command

```
forgraph price-hdroom: kdensity @,
```

which gives Figure 2.



Figure 2. Four kernel density estimates.

Note that the phrase "Kernel estimates" is displayed by kdensity in each plot. This looks rather ugly. Also the labels are not quite readable. We may improve the quality of the plot as follows

forgraph price-hdroom, margin(10) title(Kernel estimates) tsize(200): kdensity @, ti(".") xlab ylab

which gives Figure 3.



Figure 3. A more readable version of Figure 2.

forgraph has options margin, title, and tsize to specify the width between the subplots in the combined plot, the title for the combined plot, and the textsize used in the subplots. Finally, forgraph supports an option saving to save the combined plot as a gph file.

Syntax

```
forgraph list [, title(str) margin(#) tsize(#) saving(filename) for_options] : graphics_cmd
```

Example

A last illustration of forgraph demonstrates how it can be used to prepare graphs separately for subgroups of the data. Stata's default display for twoway plots with the by option is particularly attractive. Also, some of Stata's graphics commands do not support the by option. To illustrate, we do a scatterplot of price versus mpg highlighting the first four types of foreign cars:

. sort rep78 . gen rep781 = rep78

```
STB-49
```

```
. replace rep781 = . if rep78==5
. hilite price mpg, hilite(foreign) gap(4) ylab by(rep781) border saving(forgraph4, replace)
```

which gives Figure 4.



Figure 4. Using the hilite command.

Then

. forgraph 1-4, lt(num) ti(foreign cars highlighted) mar(10) ts(200): > hilite price mpg if rep78==0, hilite(foreign) gap(4) ylab border t1(repair record 0)

which gives Figure 5.



Figure 5. Using hilite and forgraph

Remark

When I decided to write a special version of for for graphics commands, I thought about extending the for command with an option graph and the other options that I added in forgraph. The reason is, simply, that I am somewhat scared by the proliferation of variants of standard Stata commands that add relatively minor functionality, or package combinations of standard Stata commands. When StataCorp publishes an updated version of the standard command, the variant becomes outdated. Clearly, I would much welcome that StataCorp would include my graphics extension in for in a future release. But, maybe it is more important that StataCorp works at modifying the Stata system to support object-oriented programming so that a user command can *inherit* all properties of parent commands. This, I realize, would not be a trivial piece of work for StataCorp, but it will make Stata easier to maintain in the long run.

gr37	Cumulative distribution function plots
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A plot of the empirical cumulative distribution function of a variable is a convenient way of looking at the empirical distribution without having to choose bins, as in histograms. The Stata command cumul is rather primitive, and a new command

cdf is offered as an alternative. With cdf, distributions can be compared within subgroups defined by a second variable, and the best fitting normal (Gaussian) model can be superimposed over the empirical cdf.

Syntax

cdf varname [weight] [if exp] [in range] [, by(varname) <u>normal samesd graph_options</u>]

aweights, fweights, iweights, and pweights are allowed.

Options

by(varname) causes a separate cdf to be calculated for each value of varname, on the same graph.

normal causes a normal probability curve with the same mean and standard deviation to be superimposed over the cdf.

- samesd is relevant only when by and normal options are used together. It fits normal curves with different means but the same standard deviations, demonstrating the fit of the Gaussian location shift model.
- graph_options are allowed. Default labeling is supplied when graph_options are absent, but the x-axis label may be supplied in the b2 graphics option and the y-axis may be labeled using the 11 option. If the xlog option is used, the normal option causes log normal distributions to be fitted.

Examples

The data refer to numbers of t4 cells in blood samples from 20 patients in remission from Hodgkin's disease and 20 patients in remission from disseminated malignancies. They are taken from Practical Statistics for Medical Research by Altman (see Shapiro et al. 1986). The two variables are t4 for the count and grp, coded 1 or 2. The command

. cdf t4, by(grp) xlab ylab

produces the graph in Figure 1. The second cdf has been leaned on relative to the first which suggests using the log T4 cell count.



Figure 1. cdf for t4 cell counts for two types of patients

The commands

```
. gen logt4=log(t4)
. cdf logt4, by(grp) xlab ylab
```

produce the graph in Figure 2, while

. cdf logt4, by(grp) normal same xlab ylab

gives Figure 3.



Reference

Shapiro et al. 1986. Practical Statistics for Medical Research. American Journal of Medical Science 293: 366-370.

sbe27	Assessing confounding effects in epidemiological studies

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In epidemiological studies, investigators sometimes lack prior knowledge about whether a covariate is a confounder and thus employ a strategy that uses the data to help them decide whether to adjust for a variable (Maldonado and Greenland 1993). With the change-in-estimate approach, a variable is selected for control only if its control seems to make a substantial difference in the exposure effect estimates. Depending on the study design and characteristics of the data, we may use logistic regressions, Poisson regressions, or Cox proportional hazard models to estimate the effect of exposure and to adjust for confounding. The effect estimates (EE) can be odds ratio (OR), rate ratio (RR) or hazard ratio (HR). In this insert we present the command epiconf which calculates and graphs adjusted effect measures such as OR, RR and HR and their confidence intervals. It also calculates change-in-estimates after adding a potential confounder into the model with the forward selection approach or deleting a potential confounder from the model with the backward deletion approach. The order of variables being selected is based on the magnitude of the change-in-estimate.

epiconf uses either a forward selection or backward deletion method. The forward selection method starts from the crude estimate without adjusting for any confounder. Then epiconf adds the confounders for adjustment one-by-one in a stepwise fashion, at each step adding the covariate with the largest change-in-estimate. The backward deletion method starts with the estimate adjusted for all potential confounders. Then epiconf deletes the confounders from adjustment one-by-one in a stepwise fashion, at each step deleting the covariate with the least change-in-estimate. epiconf also reports *p*-values from the Wald type collapsibility test statistic: significance-test-of-the-change (Maldonado and Greenland 1993):

$$Change-in-estimate(\%) = \begin{cases} \frac{EE_{adj,x} - EE_{unadj,x}}{EE_{unadj,x}} \times 100\%, & \text{forward selection method} \\ \frac{EE_{unadj,x} - EE_{adj,x}}{EE_{adj,x}} \times 100\%, & \text{backward deletion method} \end{cases}$$

The exact cut-point for importance is somewhat arbitrary and may vary from study to study. epiconf provides crude, all adjusted effect estimates and change-in-estimates, which allows investigators to chose an appropriate cut-point for their own studies. Maldonado and Greenland (1993) suggested that the change-in-estimate method performed best when the cut-point for deciding whether adjusted and unadjusted estimates differ by an important amount was set to a low value (10%). A higher than conventional α level should be considered when we use the significance-test-of-the-change (0.20). Our decision about importance could also be influenced by the method (forward or backward) we choose, as shown by the example given below. A more detailed discussion on selecting confounders can be found in Rothman and Greenland (1998).

Syntax

where *yvar* is a binary outcome variable for logistic or Poisson regression, or a survival time variable for the Cox proportional hazards model. *xvar* is a binary exposure variable of interest.

Options

con(covarlist) specifies continuous potential confounding variables.

cat(covarlist) specifies nominal potential confounding variables.

model(logit|poisson|cox) specifies the regression method. The default is logit.

expos(varname) specifies a variable that reflects the amount of exposure over which the yvar events were observed for each observation. This option is only for Poisson regression.

dead(*varname*) specifies the name of a variable recording 0 if censored and nonzero (typically 1) if failure. If dead() is not specified, all observations are assumed to have failed. This option is only for Cox regression.

detail gives details at each step. The default is a summary.

nograph yields no graph.

backward specifies the selection strategy as the backward deletion method. The default is the forward selection method.

coef graphs regression coefficients instead of effect estimates.

level (#) specifies the confidence level, in percent, for confidence intervals. The default is level (95) or as set by set level.

Examples

We use a dataset (included on the accompanying diskette) providing information on association between albuminuria and risk of death in a particular population. To assess confounding effects, we use Poisson regressions in epiconf.

```
. use conf
. describe
Contains data from conf.dta
 obs:
                743
vars:
                  9
                                               22 Nov 1998 21:51
          32,692 (95.4% of memory free)
size:
                                                        _____
                 float %9.0g
                                               Death
  1. dead
  2. ab_uria
                 float %9.0g
                                               Albuminuria
                 long %12.0g
float %9.0g
  3. age
                                               Age in years
  4. sex
                                    sex
                                               SEX
                 float %9.0g
                                               Hypertension
  5. hypert
                 float %9.0g
float %9.0g
  hichol
                                               High cholesterol
  7. weight
                                               Body weight, kg
                 float %9.0g
  8. smoke
                                               smoking
  9. time
                 double %10.0g
                                               observed time
```

First we use forward selection:

. epiconf dead ab_uria, con(age weight) cat(hich hyper smoke sex) model(poisson) expos(time) Assessment of Confounding Effects Using Change-in-Estimate Method

Forward approach Potential confounders were added one at a time sequential Adj Var Rate Ratio 95% CI Crude 3.26 2.01, 5.26 +age 1.98 1.21, 3.23 -39.3 0.00000 +weight 2.22 1.34, 3.68 12.0 0.07291 +i.smoke 1.94 1.15, 3.25 -12.6 0.01962 +i.hypert 1.94 1.14, 3.30 -5.5 0.06328 +i.sex* 1.96 1.15, 3.34 0.7 0.80716	Outcome: Exposure: N =	"dead" "ab_uri 743	a"			
Adj Var Rate Ratio 95% CI	Forward appro Potential com	oach nfounders +	were ad	lded one	e at a tim	e sequentially
Adj Var Rate Ratio 95% Cl		 		W at	Change i	n Rate ratio
Crude 3.26 2.01, 5.26 . . +age 1.98 1.21, 3.23 -39.3 0.00000 +weight 2.22 1.34, 3.68 12.0 0.07291 +i.smoke 1.94 1.15, 3.25 -12.6 0.01962 +i.hichol 2.05 1.21, 3.48 6.1 0.20995 +i.hypert 1.94 1.14, 3.30 -5.5 0.06328 +i.sex* 1.96 1.15, 3.34 0.7 0.80716	Adj Var	Kate Ka 	tio 95	5% CI	%	p> z
+age1.981.21,3.23-39.30.00000+weight2.221.34,3.6812.00.07291+i.smoke1.941.15,3.25-12.60.01962+i.hichol2.051.21,3.486.10.20995+i.hypert1.941.14,3.30-5.50.06328+i.sex*1.961.15,3.340.70.80716	Crude	3.26	2.01,	5.26		·
+weight 2.22 1.34, 3.68 12.0 0.07291 +i.smoke 1.94 1.15, 3.25 -12.6 0.01962 +i.hichol 2.05 1.21, 3.48 6.1 0.20995 +i.hypert 1.94 1.14, 3.30 -5.5 0.06328 +i.sex* 1.96 1.15, 3.34 0.7 0.80716	+age	1.98	1.21,	3.23	-39.3	0.00000
+i.smoke 1.94 1.15, 3.25 -12.6 0.01962 +i.hichol 2.05 1.21, 3.48 6.1 0.20995 +i.hypert 1.94 1.14, 3.30 -5.5 0.06328 +i.sex* 1.96 1.15, 3.34 0.7 0.80716	+weight	2.22	1.34,	3.68	12.0	0.07291
+i.hichol 2.05 1.21, 3.48 6.1 0.20995 +i.hypert 1.94 1.14, 3.30 -5.5 0.06328 +i.sex* 1.96 1.15, 3.34 0.7 0.80716	+i.smoke	1.94	1.15,	3.25	-12.6	0.01962
+i.hypert 1.94 1.14, 3.30 -5.5 0.06328 +i.sex* 1.96 1.15, 3.34 0.7 0.80716	+i.hichol	2.05	1.21,	3.48	6.1	0.20995
+i.sex* 1.96 1.15, 3.34 0.7 0.80716	+i.hypert	1.94	1.14,	3.30	-5.5	0.06328
	+i.sex*	1.96	1.15,	3.34	0.7	0.80716

*Adjusted for all potential confounders

STB-49





Figure 1. The result of using forward selection.

Note that the rate ratios in the above output and figure from a forward selection method are rate ratios adjusted for the corresponding variable plus all previous variable(s) if any. Nominal variables are labeled as *i.varname*. We see that age is an important confounder that is the first to be adjusted for. Adding age into the model makes a substantial change (39.3%) in the rate ratio estimate. After the age confounding effect has been adjusted for, the rate ratio only changes slightly by adjusting for other variables. If we take 10% as a cut-point of importance, we need to adjust for age, weight and smoking. The adjusted rate ratio is 1.94 with a 95% confidence interval of (1.15, 3.25). If we take 20% as the cut-point of importance, we need only adjust for age. The adjusted rate ratio is 1.98 with 95% confidence interval (1.21, 3.23).

Next we use the backward deletion method:

. epiconf dea > model(poiss Assessment of	ad ab_uria son) expos f Confound	a, con(a s(time) ding Eff	ge wei backwa ects U	ght) cat(h rd sing Chang	ich hyper sn e-in-Estima	noke sex) te Method
Outcome: Exposure: N =	"dead" "ab_uria 743	a"				
Backward appı Potential cor	roach nfounders	were re	moved	one at a t	ime sequent:	ially
Adj Var	 Rate Rat 	;io 95	% CI	Change in %	n Rate ratio p> z	D
Adj. all -i.sex -i.hypert -weight -i.smoke -age*	1.85 1.83 1.94 1.78 1.98 3.26	1.09, 1.09, 1.15, 1.08, 1.21, 2.01,	3.13 3.09 3.25 2.93 3.23 5.26	-0.9 5.7 -8.1 11.2 64.6	0.77795 0.11986 0.22131 0.03345 0.00000	

*Crude estimate

(Graph on next page)

Potential confounders were removed one at a time sequentially



Figure 2. The result of using backward deletion.

With a backward deletion method, the rate ratio adjusted for all variables (Adj. all) is presented first. Then, epiconf deletes the nominal variable sex first because deleting it makes the least change-in-estimate (0.9%). The most important confounder (age) in terms of change in estimate is the last covariate to be deleted. If we take 10% as a cut-point of importance, we need adjust for age and smoking. The adjusted rate ratio is 1.78 with 95% confidence interval (1.08, 2.93), while if we take 20% as a cut-point of importance, we need only adjust for age. The adjusted rate ratio is 1.98 with a 95% confidence interval (1.21, 3.23).

Acknowledgment

I thank Nicholas Cox for providing a subroutine vallist and Jean Bouyer for useful suggestions.

References

Maldonado, G. and S. Greenland. 1993. Simulation study of confounder-selection strategies. *American Journal of Epidemiology* 138: 923–936. Rothman, K. J. and S. Greenland. 1998. *Modern Epidemiology*. Philadelphia: Lippincott–Raven.

sbe28	Meta-analysis of p-values

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Fisher's work on combining of p-values (Fisher 1932) has been suggested as the origin of meta-analysis (Jones 1995). However, combination of p-values presents serious disadvantages, relative to combining estimates. For example, when p-values are testing different null hypotheses, they do not consider the direction of the association combining opposing effects, they cannot quantify the magnitude of the association, nor study heterogeneity between studies. Combination of p-values may be the only available option if nonparametric analyses of individual studies have been performed or if little information apart from the p-value is available about the result of a particular study (Jones 1995).

Fisher's method

This method (Fisher 1932) combines the probabilities of several hypotheses tests, testing the same null hypothesis

$$U = -2\sum_{j=1}^{k} \ln(p_j)$$

where the p_j are the one-tailed *p*-values for each study, and *k* is the number of studies. Then *U* follows a χ^2 distribution with 2k degrees of freedom. This method is not suggested to combine a large number of studies because it tends to reject the null hypothesis routinely (Rosenthal 1984). It also tends to have problems combining studies that are statistically significant, but in opposite directions (Rosenthal 1980).

Edgington's methods

The first method (Edgington 1972a) is based on the sum of probabilities

$$p = \left(\sum_{j=1}^{K} p_j\right)^k / k!$$

The results obtained are similar to Fisher's method, but it is also restricted for a small number of studies. This method presents problems when the sum of probabilities is higher than one; in this situation the combined probability tends to be conservative (Rosenthal 1980).

An alternative method was also suggested by Edgington (1972b), to combine more than four studies, based on the contrast of the *p*-value average

$$\overline{p} = \sum_{j=1}^{k} p_j / k$$

in which case $U = (0.5 - \overline{p})\sqrt{12}$ follows a normal distribution.

Syntax

The command metap works on a dataset containing the *p*-values for each study. The syntax is as follows:

_

_ _

Options

e(#) combines the p-values using Edgington's methods. Here, two alternatives are available; specifying a means that the additive method based on the sum of probabilities is used, while n specifies that the normal curve method based on the contrast of the *p*-value average is used. By default, Fisher's method is used.

Example

We consider data from seven placebo-controlled studies on the effect of aspirin in preventing death after myocardial infarction. Fleiss (1993) published an overview of these data. Let us assume that each study included in the meta-analysis is testing the same null hypothesis H_0 : $\theta \leq 0$ versus the alternative H_1 : $\theta > 0$. If the estimate of the log odds ratio and its standard error is available, then one-tailed *p*-values can easily be generated using the normprob function:

	generate	pvar=normp	prob(-log	rr/logse)
	list stu	dyid logrr	logse pva	ar, noobs
5	studyid	logrr	logse	pvar
	MCR-1	0.3289	0.1972	.0476728
	CDP	0.3853	0.2029	.0287845
	MRC-2	0.2192	0.1432	.0629185
	GASP	0.2229	0.2545	.1905599
	PARIS	0.2261	0.1876	.1140584
	AMIS	-0.1249	0.0981	.8985248
	ISIS-2	0.1112	0.0388	.0020786

In this situation, all methods to combine *p*-values produce similar results:

. metap pvar								
Meta-analysis of p_values								
Method		chi2	p_value	studies				
Fisher		38.938235	.00037283	7				
. metap pvar, e(a) Meta-analysis of p_values								
Method	p_value	studies						
Edgington, additive 00157658 7								
. metap pvar, e(n) Meta-analysis of p_values								
Method		Z	p_value	studies				
Edgington, Normal		2.8220842	.00238563	7				

These figures agree with the result obtained using the meta command introduced in Sharp and Sterne (1998) on a fixed effects (z = 3.289, p = 0.001) and random effects (z = 2.093, p = 0.036) models, respectively. However, the combination of *p*-values presents the serious limitations described previously.

Individual or frequency records

As for other meta-analysis commands, metap works on data contained in frequency records, one for each study or trial.

Saved results

metap saves the following results:

- S_1 Method used to combine the *p*-values
- S_2 number of studies
- S_3 Statistic used to obtain the combined probability
- S_4 Values of the statistic described in S_3
- S_5 Combined probability

References

Edgington, E. S. 1972a. An additive method for combining probability values from independent experiments. Journal of Psychology 80: 351-363.

----. 1972b. A normal curve method for combining probability values from independent experiments. Journal of Psychology 82: 85–89.

Fisher, R. A. 1932. Statistical Methods for Research Workers. 4th ed. London: Oliver & Boyd.

Fleiss, J. L. 1993. The statistical basis of meta-analysis. Statistical Methods in Medical Research 2: 121-149.

Jones, D. 1995. Meta-analysis: weighing the evidence. Stat Med 14: 137-149.

Rosenthal, R. (Ed.) 1980. New Directions for Methodology of Social and Behavioral Science. Vol. V. San Francisco: Sage.

Rosenthal, R. 1984. Valid interpretation of quantitative research results. In New Directions for Methodology of Social and Behavioral Science: Forms of Validity in Research, 12, ed. D. Brinberg and L. Kidder. San Francisco: Jossey–Bass.

Sharp, S. and J. Sterne. 1998. sbe16.1: New syntax and output for the meta-analysis command. Stata Technical Bulletin 42: 6-8.

sg64.1	Update to pwcorrs		
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This update corrects a problem in pwcorrs, see Wolfe (1997). When the option vars() was not specified and bonferroni or sidak was specified, the program reported *p*-values of 0.0000 instead of the correct values.

Reference

Wolfe, F. 1997. sg64: pwcorrs: An enhanced correlation display. Stata Technical Bulletin 35: 22-25. Reprinted in Stata Technical Bulletin Reprints, vol. 6, pp. 163-167.

sg81.1 Multivariable fractional polynomials: update

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Introduction

Multivariable fractional polynomials (FPs) were introduced by Royston & Altman (1994) and implemented in a command mfracpol for Stata 5 by Royston and Ambler (1998). The model selection procedure in the Stata 5 version was essentially the backward elimination algorithm described by Royston and Altman (1994) with modifications described by Sauerbrei and Royston (1999) (see the technical note below). An application of multivariable FPs in modeling prognostic and diagnostic factors in breast cancer is given by Sauerbrei and Royston (1999) (see our example below).

Briefly, fractional polynomial models are especially useful when one wishes to preserve the continuous nature of the predictor variables in a regression model, but suspects that some or all the relationships may be nonlinear. Using a backfitting algorithm, mfracpol finds a fractional polynomial transformation for each continuous predictor, fixing the current functional forms of the other predictor variables. The algorithm terminates when the functional forms of the predictors do not change.

Commands stfracp and stmfracp implementing respectively univariate and multivariable FPs for the survival (st) data format were presented by Royston (1998).

The present insert has two main purposes:

- 1. To update mfracpol, stfracp and stmfracp for Stata 6.
- 2. To describe improved FP model selection algorithms in mfracpol.

We have kept the same name (mfracpol) for the multivariable FP command.

The syntax of stfracp and stmfracp is unchanged, except that both programs inherit the rich set of options available with stcox in Stata 6. The syntax of mfracpol is basically as described by Royston & Ambler (1998). Changes are summarized below.

Changes to mfracpol

The main differences between the previous and new versions of mfracpol are as follows:

- 1. The new version is compatible only with Stata 6. It does not work with Stata 5.
- 2. The default model selection algorithm has been changed.
- 3. The new options: adjust(), dfdefault(), sequential, xorder(), xpowers() are available.
- 4. FPs of degree higher than 2 are supported via the df() and dfdefault() options.
- 5. The default operation of the df() option has been altered.
- 6. The screen display of the convergence process of the algorithm has been altered.
- 7. New variables created by mfracpol are named according to the conventions used by fracpoly.

Syntax of the mfracpol command

See the help file for full details. The default degrees of freedom (df) for a predictor are assigned by the df() option according to the number of distinct (unique) values of the predictor as shown in the following table.

No. of distinct	Default df
values	
1	(invalid, must be >1)
2-3	1 (straight line model)
4–5	<pre>min(2, dfdefault(#))</pre>
≥ 6	dfdefault(#)

dfdefault(#) determines the default maximum df for a predictor, the default # being 4 (second degree FP). The adjust() option works in the same way as the adjust() option in fracpoly. The default is adjust(mean) unless the predictor is binary, in which case adjustment is to the lower of the two distinct values. The xorder(*order*) option allows you to change the ordering of covariates presented to the selection algorithm. *order* may be + (the default, with the most significant predictor in a multiple linear regression model taken first), - (reverse of +, with the least significant predictor taken first) or n (no ordering, i.e., the predictors are taken in the order specified by *xvarlist*). The xpowers() option allows you to specify customized powers for any subset of the continuous predictors.

Example

We illustrate two of the analyses performed by Sauerbrei and Royston (1999). We use brcancer.dta which contains prognostic factors data from the German Breast Cancer Study Group of patients with node-positive breast cancer. The dataset was downloaded in text form from web site http://www.blackwellpublishers.co.uk/rss/. The response variable is recurrence-free survival time (rectime) and the censoring variable is censrec. There are 686 patients with 299 events. We use Cox regression to predict the log hazard of recurrence from prognostic factors of which 5 are continuous (x1, x3, x5, x6, x7) and 3 are binary (x2, x4a, x4b). Hormonal therapy (hormon) is known to reduce recurrence rates and is forced into the model. We use mfracpol to build a model from the initial set of 8 predictors using the backfitting model selection algorithm. We set the nominal *p*-value for variable and for FP selection to 0.05 for all variables except hormon for which it is set to 1:

. mfracpol cox rectime x1 x2 x3 x4a x4b x5 x6 x7 hormon, dead(censrec) > alpha(.05) select(.05, hormon:1) Deviance for model with all terms untransformed = 3471.637, 686 observations Variable Model (vs.) Deviance Dev diff. P Powers (vs.) _ _ _ _ _ _ _ ____ x5 (null) 3503.610 61.366 0.000 .5 3 m=2 (lin.) 3471.637 29.393 0.000 .5 3 1 (m=1) 3449.203 6.959 0.031 .53 0 x5 final 3442.244 .5 3 -2.5 x6 m=2 (null) 3464.113 29.917 0.000 (lin.) 3442.244 8.048 0.045 -2.5 1 (m=1) 3435.550 1.354 0.508 -2.5 .5 3435.550 x6 final .5 [hormon included with 1 df in model] lin. (null) 3440.749 x4a 5.199 0.023 1 final 3435.550 x4a 1 m=2 (null) 3436.832 xЗ 3.560 0.469 -23 xЗ final 3436.832 . x2 lin. (null) 3437.589 0.756 0.384 1 3437.589 x2 final x4b lin. (null) 3437.848 0.259 0.611 1 final 3437.848 x4b m=2 (null) 3437.893 18.085 0.001 -2 -.5 x1 (lin.) 3437.848 18.040 0.000 -2 -.5 1 3433.628 13.820 0.001 -2 -.5 (m=1) -2 3419.808 -2 -.5 x1 final x7 m=2 (null) 3420.805 3.715 0.446 -.5 3 . x7 final 3420.805 _____ _____ Cycle 1: deviance = 3420.805 _____ _____ (null) 3494.867 74.143 0.000 -2 -1 x5 m=2 31.071 0.000 -2 -1 (lin.) 3451.795 1 (m=1) 3428.023 7.299 0.026 -2 -1 0 x5 final 3420.724 -2 -1 m=2 x6 (null) 3452.093 32.704 0.000 0 0 (lin.) 3427.703 8.313 0.040 0 0 1 (m=1) 3420.724 1.334 0.513 0 0 .5 x6 final 3420.724 .5 [hormon included with 1 df in model] lin. (null) 3425.310 x4a 4.586 0.032 1 3420.724 x4a final 1 m=2 (null) 3420.724 xЗ 5.305 0.257 -.5 0 xЗ final 3420.724 x2 lin. (null) 3420.724 0.214 0.644 1 3420.724 x2 final lin. (null) 3420.724 0.145 0.703 x4b 1 3420.724 final x4b m=2 (null) 3440.057 19.333 0.001 -2 -.5 x1 -2 -.5 (lin.) 3440.038 19.314 0.000 1 16.225 0.000 3436.949 -2 -.5 (m=1) -2 x1 final 3420.724 -2 - .5x7 m=2 (null) 3420.724 2.152 0.708 -13 . x7 final 3420.724

Fractional polynomial fitting algorithm converged after 2 cycles.

Transformations of covariates:

- \rightarrow gen double Ix1_1 = X^-2-.0355 if e(sample)
- -> gen double Ix1__2 = X^-.5-.4342 if e(sample)
 (where: X = x1/10)
- -> gen double $Ix5_1 = X^{-2}-3.984$ if e(sample)
- \rightarrow gen double Ix5__2 = X^-1-1.996 if e(sample)
- (where: X = x5/10)
- -> gen double Ix6__1 = X^{.5-.3332} if e(sample)
 (where: X = (x6+1)/1000)

Variable		-Initial-			-Final-			
	df	Select	Alpha	Status	df	Powers		
x1	4	0.0500	0.0500	in	4	-25		
x2	1	0.0500	0.0500	out	0			
xЗ	4	0.0500	0.0500	out	0			
x4a	1	0.0500	0.0500	in	1	1		
x4b	1	0.0500	0.0500	out	0			
x5	4	0.0500	0.0500	in	4	-2 -1		
x6	4	0.0500	0.0500	in	2	.5		
x7	4	0.0500	0.0500	out	0			
hormon	1	1.0000	0.0500	in	1	1		
Cox regres Entry time	ssion H e O	Breslow me	ethod for	ties	Nu LR Pr	mber of c chi2(7) ob > chi2	obs = = 2 =	686 155.62 0.0000
Cox regres Entry time Log likeli	ssion H e O ihood = -1	3reslow me 1710.3619	ethod for	ties	Nu LR Pr Ps	mber of c chi2(7) ob > chi2 eudo R2	obs = = 2 = =	686 155.62 0.0000 0.0435
Cox regres Entry time Log likeli 	ihood = -1	3reslow me 1710.3619	ethod for	ties	Nu LR Pr Ps	mber of c chi2(7) ob > chi2 eudo R2 	bs = = 2 = =	686 155.62 0.0000 0.0435
Cox regres Entry time Log likeli rectime censrec	ihood = -1 Coe	3reslow me 1710.3619 	ethod for	ties z	Nu LR Pr Ps P> z	mber of c chi2(7) ob > chi2 eudo R2 [95	bbs = = 2 = = 5% Conf.	686 155.62 0.0000 0.0435 Interval]
Cox regres Entry time Log likeli rectime censrec Ix1_1	ssion H o 0 hhood = -1 Coe + 44.73:	3reslow me 1710.3619 2f. Std 	ethod for . Err. 56682	ties z 5.418	Nu LR Pr Ps 	mber of c chi2(7) ob > chi2 eudo R2 [95 28.	bbs = = 2 = 5% Conf. 55097	686 155.62 0.0000 0.0435 Interval]
Cox regres Entry time Log likeli rectime censrec Ix1_1 Ix1_2	ssion H o 0 hhood = -1 Coe 	Breslow me 1710.3619 ef. Std 	ethod for . Err. 56682 09611	ties z 5.418 -4.584	Nu LR Pr Ps P> z 0.000 0.000	mber of c chi2(7) ob > chi2 eudo R2 [95 	bbs = = = % Conf. 55097 58571	686 155.62 0.0000 0.0435
Cox regres Entry time Log likeli rectime censrec Ix1_1 Ix1_2 x4a	ssion H o 0 hood = -1 Coe 44.733 -17.923 .50069	3reslow me 1710.3619 9f. Std 	ethod for . Err. 56682 29611 96324	ties z 5.418 -4.584 2.006	Nu LR Pr Ps 	mber of c chi2(7) ob > chi2 eudo R2 [95 28. -25. .01	bbs = = = 5% Conf. 55097 58571 14276	686 155.62 0.0000 0.0435 Interval] 60.91657 -10.26032 .9899687
Cox regres Entry time Log likeli rectime censrec Ix1_1 Ix1_2 x4a Ix5_1	ihood = -1 	3reslow me 1710.3619 2f. Std 377 8.29 302 3.90 302 2.249 904 .007	ethod for . Err. . Err. . 56682 09611 96324 76972	z 5.418 -4.584 2.006 5.040	Nu LR Pr Ps 	mber of c chi2(7) ob > chi2 eudo R2 	bbs = 2 = 55097 58571 14276 237041	686 155.62 0.0000 0.0435
Cox regres Entry time Log likeli 	ihood = -1 cod cod cod cod cod cod cod cod cod cod	3reslow me 1710.3619 \$f. Std 377 8.29 302 3.90 302 3.90 302 .249 904 .007 645 .086	ethod for . Err. 56682 29611 96324 76972 54255	z 5.418 -4.584 2.006 5.040 -6.353	Nu LR Pr Ps 0.000 0.000 0.045 0.000 0.000	mber of c chi2(7) ob > chi2 eudo R2 [98 -25. .01 .02 .02 .02 .02	bbs = = 2 = 5% Conf. 55097 58571 14276 14276 137041 84554	686 155.62 0.0000 0.0435 Interval] 60.91657 -10.26032 .9899687 .0538767 3796736
Cox regres Entry time Log likeli 	ihood = -1 ihood = -1 	3reslow me 1710.3619 af. Std 377 8.29 302 3.99 982 .244 904 .007 545 .086 966 .350	ethod for . Err. . 56682 09611 096324 76972 54255 06314	ties z 5.418 -4.584 2.006 5.040 -6.353 -5.153	Nu LR Pr Ps 0.000 0.000 0.045 0.000 0.000 0.000 0.000	mber of c chi2(7) ob > chi2 eudo R2 28. -25. .01 .02 71 -2.4	bbs = = 2 = 55097 58571 14276 237041 84554 194191	686 155.62 0.0000 0.0435 Interval] 60.91657 -10.26032 .9899687 .0538767 3796736 -1.119741

Final multivariable fractional polynomial model for rectime

Deviance: 3420.724.

Some explanation of the output from the model selection algorithm is desirable. Consider the first few lines of output in the iteration log:

1.	Deviance	for mo	del wit	h all term	s untransf	ormed =	3471.637,	686 observations
	Variable	Model	(vs.)	Deviance	Dev diff.	Ρ	Powers	(vs.)
2.	x5	m=2	(null)	3503.610	61.366	0.000	.5 3	•
3.			(lin.)	3471.637	29.393	0.000	.5 3	1
4.			(m=1)	3449.203	6.959	0.031	.5 3	0
5.	x5	final		3442.244			.5 3	

Line 1 gives the deviance $(-2 * \log \text{ partial likelihood})$ for the Cox model with all terms linear, showing where the algorithm starts. The model is modified variable-by-variable in subsequent steps. The most significant linear term turns out to be x5 which is therefore processed first. Line 2 compares the best-fitting FP with m = 2 for x5 with a model omitting x5. The FP has powers (0.5,3) and the test for inclusion of x5 is highly significant. The reported deviance of 3503.610 is for the null model, not for the model with m = 2. The deviance for the m = 2 model may be calculated by subtracting the deviance difference (Dev diff.) from the reported deviance, giving 3503.610 - 61.366 = 3442.244. Line 3 shows that the m = 2 model is also a highly significantly better fit than a straight line (lin.) and line 4 that it is also somewhat better than an FP with m = 1 (P = 0.031). Thus at this stage in the model selection procedure the final model for x5 (line 5) is an FP with powers (0.5,3). The overall model with m = 2 for x5 and all other terms linear has deviance 3442.244.

After all the variables have been processed (cycle 1) and reprocessed (cycle 2) in this way, convergence is achieved since the functional forms (FP powers and variables included) after cycle 2 are the same as after cycle 1. The model finally chosen is Model II as given in Tables 3 and 4 of Sauerbrei and Royston (1999). Due to scaling of variables, the regression coefficients reported there are different, but the model and its deviance are identical. It includes x1 with powers (-2, -0.5), x4a, x5 with powers (-2, -1), and x6 with power 0.5. There is strong evidence of nonlinearity for x1 and for x5, the deviance differences for comparison with a straight line model (m=2 vs lin.) being respectively 19.3 and 31.1 at convergence (cycle 2). Predictors x2, x3, x4b and x7 are dropped, as may be seen from their status out in the table Final multivariable fractional polynomial model for rectime.

Note that all predictors except x4a and hormon (which are binary) have been adjusted to the mean of the original variable. For example, the mean of x1 (age) is 53.05 years. The first FP transformed variable for x1 is $x1^{-2}$ and is created by the expression gen double $Ix1_1 = X^{-2}$. 0355 if e(sample). The value .0355 is obtained from $(53.05/10)^{-2}$. The division by 10 is applied automatically to improve the scaling of the regression coefficient for $Ix1_1$.

According to Sauerbrei and Royston (1999), medical knowledge dictates that the estimated risk function for x5 (number of positive nodes), which was based on the above FP with powers (-2, -1), should be monotonic, but it was not. They improved Model II by estimating a preliminary exponential transformation $x5e = \exp(-0.12 \times x5)$ for x5 and fitting a degree 1 FP for x5e, thus obtaining a monotonic risk function. The value of -0.12 was estimated univariately using nonlinear Cox regression with the ado-file boxtid (Royston and Ambler 1999). To ensure a negative exponent Sauerbrei and Royston (1999) restricted the powers for x5e to be positive. Their Model III may be estimated using the following command:

> . mfracpol cox rectime x1 x2 x3 x4a x4b x5e x6 x7 hormon, dead(censrec) > alpha(.05) select(.05, hormon:1) df(x5e:2) xpowers(x5e:0.5 1 2 3)

Other than the customization for x5e, the command is the same as before. The resulting model is as reported in Table 4 of Sauerbrei and Royston (1999):

Final mult	tivariable	e fraction	nal polyr	nomial moc	lel for	rectime		
Variable		-Initial-			-Final-			
	df	Select	Alpha	Status	df	Powers		
x1	+ 4	0.0500	0.0500	in	4	-25		
x2	1	0.0500	0.0500	out	0			
xЗ	4	0.0500	0.0500	out	0			
x4a	1	0.0500	0.0500	in	1	1		
x4b	1	0.0500	0.0500	out	0			
x5e	2	0.0500	0.0500	in	1	1		
x6	4	0.0500	0.0500	in	2	.5		
x7	4	0.0500	0.0500	out	0			
hormon	1	1.0000	0.0500	in	1	1		
Entry time Log likel:	e 0 ihood = -1	1711.6186			Nu LR Pr Ps	mber of obs chi2(6) ob > chi2 eudo R2	= = =	686 153.11 0.0000 0.0428
rectime censrec	 Coe	ef. Std	. Err.	z	P> z	[95%	Conf.	Interval]
Ix11	43.55	382 8.2	53433	5.277	0.000	27.37	 738	59.73025
$Ix1_2$	-17.48	136 3.9	11882	-4.469	0.000	-25.14	851	-9.814212
x4a	.51743	.24	93739	2.075	0.038	.0286	713	1.006199
Ix5e1	-1.9812	213 .22	68903	-8.732	0.000	-2.425	909	-1.536516
Ix61	-1.840	.35	08432	-5.245	0.000	-2.52	772	-1.15244
hormon	39449	998 .1	28097	-3.080	0.002	6455	654	1434342

Deviance: 3423.237.

Technical note: Model selection procedures

Sauerbrei and Royston (1999)'s modifications to the algorithm of Royston and Altman (1994) were (a) to order the variables initially according to decreasing significance in a multiple linear regression model, and (b) to allow variables to have customized powers in special situations. As described above, Sauerbrei and Royston (1999) used the latter feature when modeling a variable which had been subjected to a preliminary transformation.

In what follows, we describe model selection procedures for a single continuous covariate x which represent one step of the iterative algorithm just exemplified. In each procedure, a significance level α_{sel} is chosen for testing for inclusion of x and another, $\alpha_{\rm FP}$, for comparisons between FP models. A variable x is forced into the model by setting $\alpha_{\rm sel} = 1$. It is forced to assume the most complex functional form (i.e., highest degree FP) allowed for it by setting $\alpha_{\rm FP} = 1$. Theoretically, any combination of α_{sel} and α_{FP} is possible, though in practice only a few choices are reasonable. For example, the choice $\alpha_{sel} = 1$, $\alpha_{FP} = 0.05$ (the default in mfracpol) includes x in the model and allows simplification of its functional form. The choice $\alpha_{sel} = \alpha_{FP} = 0.05$ additionally allows x to be dropped if it fails an overall test of significance at the 5% level. Full models may be built by taking $\alpha_{sel} = \alpha_{FP} = 1$. The combination $\alpha_{sel} = 0.05$, $\alpha_{FP} = 1$ is unlikely to be much used since x is either rejected or allowed full complexity, which seems rather perverse.

The null distribution of the likelihood-ratio statistic used in the significance tests is assumed to be F for normally distributed data, χ^2 in other cases. In the descriptions below, the most complex model allowed for x is taken to be an FP with m = 2, though the extension to m > 2 is obvious. Note that with the present update of mfracpol the complexity is not limited to m = 2; FP models with m > 2 are supported via the df() and dfdefault() options.

Previous procedure

In the earlier version of mfracpol, Royston and Ambler (1998) incorporated an initial variable inclusion step to reduce the Type I error rate. The procedure was as follows:

- 1. Perform a 4 df test at the α_{sel} level of the best-fitting second-degree FP against the null model. If the test is not significant, drop x and stop, otherwise continue.
- 2. Perform a 2 df test at the α_{FP} level of the best-fitting FP of degree 2 against the best FP of degree 1. If the test is significant, stop (the final model is the FP with m = 2), otherwise continue.
- 3. Perform a 1 df test at the α_{FP} level of the best-fitting FP of degree 1 against a straight line. The final model is the FP with m = 1 if the test is significant, otherwise it is a straight line.

When $\alpha_{sel} = 1$, step 1 is omitted. The main problem with this algorithm is that it can give illogical results. For example, it may happen that the inclusion test (step 1) is significant but that none of the subsequent tests (m = 2 vs m = 1, m = 1 vs straight line, or in fact straight line vs null, which is not formally part of the procedure) is significant. In this situation the procedure selects a straight line, which may even be the model least strongly supported by the data.

New default procedure

The model selection procedure described by Royston and Sauerbrei (1999) is implemented as the default in the present version of mfracpol. It has the flavor of a closed test (CT) procedure (Marcus et al. 1976) which maintains approximately the correct Type I error rate for each component test. The procedure allows the complexity of candidate models to increase progressively from a prespecified minimum—a null model if $\alpha_{sel} < 1$, or a straight line if $\alpha_{sel} = 1$ —to a prespecified maximum—an FP—according to an ordered sequence of test results. The procedure is as follows:

- 1. Perform a 4 df test at the α_{sel} level of the best-fitting second-degree FP against the null model. If the test is not significant, drop x and stop, otherwise continue.
- 2. Perform a 3 df test at the α_{FP} level of the best-fitting second-degree FP against a straight line. If the test is not significant, stop (the final model is a straight line), otherwise continue.
- 3. Perform a 2 df test at the α_{FP} level of the best-fitting second-degree FP against the best-fitting first-degree FP. The final model is the FP with m = 2 if the test is significant, the FP with m = 1 if not.

The tests at steps 1, 2 and 3 are of overall association, nonlinearity and between a simpler or more complex FP model, respectively. When $\alpha_{sel} = 1$, step 1 is omitted.

The sequential procedure

For completeness and to facilitate further study, mfracpol with the sequential option performs Sauerbrei and Royston's (1999) version of Royston and Altman (1994)'s algorithm, which is as follows:

- 1. Perform a 2 df test at the α_{FP} level of the best-fitting FP of degree 2 against the best FP of degree 1. If the test is significant, stop (the final model is the FP with m = 2), otherwise continue.
- 2. Perform a 1 df test at the α_{FP} level of the best-fitting FP of degree 1 against a straight line. If the test is significant, stop (the final model is the FP with m = 1), otherwise continue.
- 3. Perform a 1 df test at the α_{sel} level of a straight line against the model omitting x. If the test is significant, the final model is a straight line, otherwise omit x.

When $\alpha_{sel} = 1$, the final step is omitted.

Because several tests are carried out, when the true relationship is a straight line, the actual Type I error rate considerably exceeds the nominal value of α_{FP} (Ambler and Royston 1999). The procedure therefore tends to favor more complex models over simple ones and may be expected to overfit the data more than the new default procedure.

Acknowledgment

This work received financial support from project grant number 045512/Z/95/Z from the Wellcome Trust. We thank Dr. W. Sauerbrei for helpful comments on the manuscript.

References

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- Marcus, R., E. Peritz, and K. R. Gabriel. 1976. On closed test procedures with special reference to ordered analysis of variance. *Biometrika* 76: 655-660.

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Royston, P. and D. G. Altman. 1994. Regression using fractional polynomials of continuous covariates: parsimonious parametric modelling (with discussion). Applied Statistics 43: 429–467.

Royston, P. and G. Ambler. 1998. sg81: Multivariable fractional polynomials. Stata Technical Bulletin 43: 24-32.

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This revision of outreg adds enhancements and corrects a number of problems with the previous version in Gallup (1998). outreg has also been updated for Stata 6.0 and made more efficient because Stata has made fundamental changes in the way it reports estimation results (a great improvement).

outreg has several new capabilities. One can now:

- Choose different numbers of decimal places for each coefficient with the bdec option.
- Report the extra statistics appended to the e(b) matrix with the xstats option.
- Choose either single column or multiple column formatting for multi-equation estimation with the onecol option.
- Report *p*-values under coefficients with the *pvalue* option.
- Report the exponentiated form of coefficients in logit, clogit, mlogit, glogit, cox, xtprobit, xtgee, or any other command with the eform option.
- varlists can be specified for multivariate regressions.

Included with the current insert is a version of the outreg command written in Stata 5.0, outreg5, for backwards capability for those who have not upgraded yet, and for use with older routines that have not been updated for Stata 6.0 such as dprobit2, dlogit2, and dmlogit2. Given the major changes in the way Stata 6.0 reports results, it does not make sense to have a single outreg command that can work with both versions of Stata. There are probably still some Stata 5.0 estimation commands for which outreg5 will not work correctly. Users of Stata 5.0 with the original outreg should switch to outreg5 because it fixes a number of bugs in the original outreg.

As for those bugs, the most important was that the critical values used for determining asterisks to indicate significance levels were incorrect for nonlinear estimation (I didn't notice that invt is two-tailed, but invnorm is one-tailed). Also, despite my claims to the contrary, the original outreg did not work correctly with all Stata estimation commands. I have now tested outreg with all the commands. Please let me know if I have not tested thoroughly enough.

Reference

Gallup, J. L. 1998. sg97: Formatting regression output for published tables. Stata Technical Bulletin 46: 28.

sg107.1	Generalized Lorenz curves and related graphs

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A bug affecting the behavior of glcurve in some special cases has been found and fixed.

sg111	A modified likelihood-ratio test command

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Stata's lrtest command compares nested models estimated by maximum likelihood through the likelihood-ratio test (McCullagh and Nelder 1989) using a backward strategy; that is, to test if adding one or more variables improves the fit of the regression model. First the complete model containing all variables of interest must be estimated. The second model must be reduced and nested within the first, excluding those variables of interest. However, for nonstatisticians, a forward strategy seems more intuitive, that is, fitting the simplest model first and then testing the inclusion of the variable(s) of interest after that.

The lrtest2 command presented in this insert is a simple modification of the original lrtest command, to perform the likelihood-ratio test under a forward strategy, although a backward strategy is also permitted.

Syntax

The lrtest2 command has the same syntax and options as lrtest.

Example

Using the low birth weight data discussed in the Stata manual in the documentation for lrtest, we first fit a model adjusted by race, smoke and uterine irritability (ui).

```
. use birthwt
. describe
Contains data from birthwt.dta
  obs: 189
 vars:
                     10
                                                         30 Jan 1998 12:59
             15,876 (98.3% of memory free)
 size:
                                 ------
   1. low double %9.0g
                                           birth weight less than 2.5kg (0
                  double %9.0g
                                                        age of mother in years
   2. age
   3. lwt
                  double %9.0g
                                                         weight of mother (lbs) last men
                                               white/black/other
white/black/other
smoking status during the pregn
number of previous premature la
history of hypertension (0/1)
has uterine irritability
number of physician visits in f
                   double %9.0g
   4. race
   5. smoke double %9.0g
   6. ptl
                 double %9.0g
   7. ht
                   double %9.0g
                   double %9.0g
   8. ui
                  double %9.0g
   9. ftv
                                                         number of physician visits in f
                   double %9.0g
  10. bwt
                                                         actual birth weight
Sorted by:
. xi: logistic low i.race smoke ui
            Irace_1-3
                                            (naturally coded; Irace_1 omitted)
i.race
Logit estimates
                                                               Number of obs =
                                                                                             189
                                                              LR chi2(4)
                                                                                  =
                                                                                          18.80
                                                              Prob > chi2
                                                                                 =
                                                                                          0.0009
                                                              Pseudo R2
Log likelihood = -107.93404
                                                                                  =
                                                                                          0.0801
      low | Odds Ratio Std. Err. z P>|z| [95% Conf. Interval]
------

        Irace_2
        3.052746
        1.498084
        2.274
        0.023
        1.166749
        7.987368

        Irace_3
        2.922593
        1.189226
        2.636
        0.008
        1.31646
        6.488269

        smoke
        2.945742
        1.101835
        2.888
        0.004
        1.41517
        6.131701

        ui
        2.419131
        1.047358
        2.040
        0.041
        1.03546
        5.651783

_____
                       _____
```

. lrtest2, saving(0)

Now, we study the improvement of the goodness of fit of the logistic regression model including the variables age, weight at last menstrual period (lwt), premature labor history (ptl) and history of hypertension (ht).

. xi: logistic low	age lwt i.race	smoke ptl ht ui		
i.race	Irace_1-3	(naturally coded; Irace_1 omit	tted)	
Logit estimates		Number of obs	=	189
		LR chi2(8)	=	33.25
		Prob > chi2	=	0.0001
Log likelihood = -1	.00.71348	Pseudo R2	=	0.1417

low	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]
age	.9732933	.0354791	-0.743	0.458	.9061816	1.045375
lwt	.9849321	.0068235	-2.192	0.028	.9716487	.9983972
Irace_2	3.536789	1.862006	2.399	0.016	1.260315	9.925202
Irace_3	2.367028	1.039593	1.962	0.050	1.000824	5.598207
smoke	2.517708	1.009244	2.303	0.021	1.14761	5.523529
ptl	1.719021	.5952396	1.565	0.118	.8720445	3.388628
ht	6.256967	4.328382	2.651	0.008	1.612606	24.27725
ui	2.135277	.9809289	1.651	0.099	.8677992	5.253991
. lrtest2						
Logistic:	likelihood-	ratio test			chi2(4) =	14.44
0					Prob > chi2 =	0.0060

The result obtained is the same as using the ltrest command, following a backward strategy, concluding that the inclusion of the variables age, lwt, ptl, and ht improves the fit of the logistic regression model.

Reference

McCullagh D. W. and J. A. Nelder. 1989. Generalized Linear Models. London: Chapman and Hall.

sg112 Nonlinear regression models involving power or exponential functions of covariates	
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Introduction

A first degree fractional polynomial (FP) is a function of the form $\beta_0 + \beta_1 x^p$, where x > 0 and p is a power chosen from the set $\mathcal{P} = \{-2, -1, -0.5, 0, 0.5, 1, 2, 3\}$. By convention, x^p with p = 0 means $\log x$. The best-fitting (maximum likelihood) value \tilde{p} of p in \mathcal{P} may be found by using the Stata command fracpoly with the option degree(1). A first degree FP is a special case of the power-function family (Box and Tidwell 1962) which is obtained when p is allowed to take any real value, i.e., is not restricted to \mathcal{P} . Power functions yield curves for $p \neq 1$ and straight lines for p = 1. For p < 0 they have an asymptote β_0 as $x \to \infty$. The main purpose of the present insert is to describe a program boxtid which finds the maximum likelihood estimate \hat{p} of p for several types of error structure, most importantly normal and binomial errors, GLMs and Cox regression. Closely related is the family of exponential functions $\beta_0 + \beta_1 \exp(px)$ which, since $\exp(px) = [\exp(x)]^p$, may be viewed as power functions on the exponential scale. boxtid also estimates these models. In addition, multivariable nonlinear models with power or exponential transformations of several x's may be estimated.

There are two main reasons why it may be useful to fit a Box-Tidwell model rather than or in addition to a first degree FP. First, the fit may be markedly better when \hat{p} lies considerably outside the interval [-2, 3] or lies between elements of \mathcal{P} . If \hat{p} is close to \tilde{p} (say, within one standard error of it), we are reassured that the FP model has not missed anything important. Since boxtid can fit continuous powers for any degree of FP, it can be used to check the appropriateness of powers for any such FP. Second, boxtid can estimate confidence intervals for p and for the fitted values $\hat{\beta}_0 + \hat{\beta}_1 x^{\hat{p}}$ which allow for the estimation of p. Confidence intervals for fitted values are really only achievable with FPs by the use of bootstrapping, which is computationally intensive and not straightforward to set up.

To demonstrate the method we give examples using the well-known auto dataset supplied with Stata, a breast cancer dataset previously analysed by Sauerbrei and Royston (1999), an IgG dataset previously analysed by Royston and Altman (1994) and a dataset of measurements of fetal growth.

The ado-file boxtid is a regression-like command with the following basic syntax:

boxtid regression_cmd yvar xvarlist [weight] [if exp] [in range] [, options]

Details are given in the section Syntax.

Example 1: Automobile data

We use boxtid to fit a Box-Tidwell model to predict mpg from weight for the dataset auto.dta as follows:

. boxtid regress mpg weight Iteration 0: Deviance = 385.8874 Iteration 1: Deviance = 385.8874 (change = -.0000794)

-> gen dou	ble Iweig_1	= X^-0	.446	06109 if	e(sample)	7)		
-> gen dou	Die iweig_2 X = weight/1	= X - 0	.446	J*In(X) = .67	51 1I e(sa	mpie)		
[Total ite	rations: 1]	000)						
- Box-Tidwel	l regression	model						
Source	SS	df		MS		Number of obs	=	74
+						F(2, 71)	=	73.33
Model	1646.43761	2	823	.218806		Prob > F	=	0.0000
Residual	797.021847	71	11.3	2256598		R-squared	=	0.6738
+						Adj R-squared	=	0.6646
Total	2443.45946	73	33.4	4720474		Root MSE	=	3.3505
mpg	Coef.	Std.	Err.	t	P> t	[95% Conf.	In	terval]
Iweig_1	63.2036	52.77	866	1.198	0.235	-42.03406	1	68.4413
Iweig_p1	0087	42.75	559	0.000	1.000	-85.26092	8	5.24352
_cons	20.42983	.5515	679	37.040	0.000	19.33004	2	1.52963
weight	0060087	.0005	179	-11.603	Nonlin.	dev. 4.890 (H	? =	0.031)
p1	4459573	.6584	836	-0.677				

Deviance: 385.887.

The estimation procedure converges after one iteration, showing that the initial value of p was very accurate. The above table shows that the maximum likelihood estimate $\hat{p} = -0.446$ (SE 0.658). The deviance of the model is 385.887. A first degree FP has $\tilde{p} = -0.5$ and a deviance of 385.894, so the two models are essentially identical in this case. The entry marked Nonlin. dev. indicates the amount of nonlinearity found in the data. In this case the deviance difference between the Box-Tidwell model and a straight line is 4.89 (P = 0.031), so there is mildly significant nonlinearity, at least in p-value terms.

Two new variables are created for each power estimated. The first (Iweig_1 above, with power p1) is the transformed predictor variable. The second (Iweig_p1 above) is an auxiliary variable used within the algorithm to estimate p. (In the above output, Iweig_p1 is initially called Iweig_2 but is immediately renamed.) At convergence the auxiliary variable has (or should have) a coefficient estimate close to zero. Its presence in the final regression model ensures that the standard errors are valid. Without it, the fitted values from the model would be the same but the standard errors would be seriously underestimated.

Figure 1 shows the observed and fitted values of mpg from the model, together with their standard errors.



Figure 1: Observed and fitted values of mpg and their standard errors from a Box-Tidwell model

The plot was obtained simply by typing fracplot (boxtid is fully compatible with the fracplot and fracpred commands in Stata 6). The nonlinearity in the relationship between mpg and weight can be clearly seen.

Figure 2 shows the standard errors of the predicted values of mpg from the FP and Box-Tidwell models plotted against weight.

(Graph on next page)



Figure 2: SEs of predicted values of mpg from FP (solid line) and Box-Tidwell (dashed line) models.

The SEs were obtained by using fracpred with the option stdp immediately after running fracpoly and boxtid. Except at car weights of 2200 and 3700 lbs, the standard errors from boxtid are markedly larger than from fracpoly, showing that the estimation of p as a continuous parameter may make a major difference.

Example 2: Recurrence-free survival time in breast cancer

The dataset consists of information on 686 patients with primary node positive breast cancer who were recruited by the German Breast Cancer Study Group (GBSG) between July 1984 and December 1989. Of these, 299 patients experienced at least one disease recurrence or died during the follow-up period. The median follow-up time was nearly 5 years. The data have been extensively analysed by Sauerbrei and Royston (1999), who used fractional polynomials to develop prognostic models. Here we consider Cox regression models for the relationship between recurrence-free survival time (rectime) with censoring variable censrec and the strongest prognostic factor, the number of positive lymph nodes (x5).

The best-fitting second degree FP has powers (1, 2) and a deviance of 3494.99. The model fits significantly better than first degree FP and Box-Tidwell models. However, the second degree FP model is a quadratic curve with a maximum log relative hazard estimated at 24 positive nodes. Such a maximum implies that the risk of disease recurrence actually decreases for patients with >24 nodes, which is strongly contrary to medical knowledge. To produce a risk curve consistent with medical knowledge, Sauerbrei and Royston (1999) fitted a univariate exponential model to obtain a preliminary transformation x5e = exp(p * x5). They then used the ado-file mfracpol (Royston and Ambler 1998, 1999) to model x5e simultaneously with other prognostic factors in a multivariable FP model.

The exponential model may be fit by boxtid using the command

```
. boxtid cox rectime x5, dead(censrec) expon(x5)
```

The estimate $\hat{p} = -0.117$ (SE 0.042). The fitted curve from this model is monotonic and has an asymptote. The deviance is 3.0 higher than that of the second degree FP. We illustrate the different fits in Figure 3.



Figure 3: Fitted log relative hazard functions from FP and Box-Tidwell (exponential) models

Example 3: Checking FP models

Breast cancer data (continued)

Sauerbrei and Royston's (1999) final model (III) may be checked using boxtid. As well as x5e, model III includes the predictors age (x1), tumor grade (x4a), progesterone receptor status (x6) and hormonal treatment status (hormon). FPs were used for x1 (-2 -0.5) and x6 (0.5), while x4a, x5e and hormon were entered as linear. We check the x5 and x6 transformations simultaneously by fitting a multivariable power and exponential model. The other predictors are entered in the model as linear terms. We fit this model using the commands

```
. fracgen x1 -2 -0.5
. boxtid cox rectime x1_1 x1_2 x4a x5 x6 hormon, dead(cens) expon(x5) df(1, x5 x6:2)
```

The value of \hat{p} for x6 is 0.256 (SE 0.181). The fitted curve for x6 is similar to that of the best-fitting first degree FP curve.

Fetal femur length data

Measurements of the femur length of 649 fetuses were obtained by ultrasound scanning of the mother's abdomen. A log transformation of femur length removes almost all of the heteroscedasticity seen in the untransformed observations. Figure 4 shows a scatter plot of log(femur length) against gestational age, with the fitted curves from a second degree FP inscribed.



Figure 4: Log transformed femur length data with fitted second degree FP

First and second degree FPs have powers \tilde{p} of -1 and (-2, 0) and deviances of -1540.02 and -1689.93 respectively. The large deviance difference of 149.91 shows that a second degree FP is a much better fit than a first degree. However, a first degree Box-Tidwell model has a deviance of -1683.99, close to that of the *second* degree FP. The power $\hat{p} = -1.39$ has SE 0.03, so here the power is very precisely estimated and is some 13 standard errors away from the first degree FP power of -1. Moreover the Box-Tidwell model is monotonic, which is appropriate for growth data since average femur length does not diminish as gestation advances. Monotonicity is not guaranteed with second degree FP models. The fitted curves from the second degree FP and first degree Box-Tidwell models are almost superimposable. In this case we conclude that a first degree Box-Tidwell model is probably preferable to a first or second degree FP model.

Immunoglobulin-G (IgG) data

The IgG data were used as an example for second degree FPs (see [R] **fracpoly**, pp. 502–504). A measurement of IgG was made on each of 298 children aged 6 months to 6 years. The outcome variable is the square root of the IgG concentration. The best-fitting second degree FP has powers (-2, 2), so the fitted model is of the form $b_0 + b_1 x^{-2} + b_2 x^2$. The best-fitting second degree Box–Tidwell model has powers (-2.58, 1.85) with very large SEs of (2.21, 1.44). The deviance difference between the FP and Box–Tidwell models is small (0.18) and the fits are almost identical. In this case we are reassured that the FP model cannot be improved by a Box–Tidwell model.

In our experience with real datasets, second degree FP models provide good coverage of the two dimensional power space and second degree Box-Tidwell models are seldom an improvement.

Syntax

boxtid regression_cmd yvar xvarlist [weight] [if exp] [in range] [, major_options minor_options

regression_cmd_options

where *regression_cmd* may be one of cox, glm, logistic, logit, poisson, regress; boxtid shares the features of all estimation commands; fracplot may be used following boxtid to show plots of fitted values and partial residuals; fracpred may be used for prediction; and all weight types supported by *regression_cmd* are allowed.

Options

The major_options (most used options) are

adjust(adj_list) df(df_list) expon(varlist)

and the minor_options are

```
<u>dfd</u>efault(#) <u>in</u>it(init_list) <u>it</u>er(#) <u>ltol</u>erance(#) powers(numlist) <u>tr</u>ace <u>zer</u>o(varlist)
```

regression_cmd_options are any of the options available with *regression_cmd*.

Major options

- adjust(adj_list) defines the adjustment for the covariates xvar1, xvar2, ..., xvarlist. The default is adjust(mean), except
 for binary covariates where it is adjust(#), # being the lower of the two distinct values of the covariate. A typical item
 in adj_list is varlist: mean|# |no. Items are separated by commas. The first item is special in that varlist: is optional, and
 if omitted, the default is (re)set to the specified value (mean or # or no). For example, adjust(no, age:mean) sets the
 default to no and adjustment for age to mean.
- df (df_list) sets up the degrees of freedom (df) for each predictor. Each power and each regression coefficient count as 1 df. Predictors specified to have 1 df are fitted as linear terms in the model. The first item in df_list may be either # or varlist :#. Subsequent items must be varlist:#. Items are separated by commas and varlist is specified in the usual way for variables. With the first type of item, the df for all predictors are taken to be #. With the second type of item, all members of varlist (which must be a subset of xvarlist) have # df.

The default df for a predictor (specified in *xvarlist* but not in df_list) are assigned according to the number of distinct (unique) values of the predictor as follows:

No. of distinct	Default df
values	
1	(not applicable)
2-3	1
4-5	<pre>min(2, dfdefault(#))</pre>
≥ 6	dfdefault(#)

expon(varlist) specifies that all members of varlist are to be modeled using exponential functions, the default being power (Box-Tidwell) functions. For each xvar in varlist, a multi-exponential model

$$\beta_1 \exp(p_1 x) + \beta_2 \exp(p_2 x) + \dots$$

is estimated.

Minor options

dfdefault(#) determines the default maximum degrees of freedom (df) for a predictor. The default is 2.

init(*init_list*) sets initial values for the power parameters of the model. By default these are calculated automatically. The first item in *init_list* may be either # [#...] or *varlist:*# [#...]. Subsequent items must be varlist:# [#...]. Items are separated by commas and *varlist* is specified in the usual way for variables. If the first item is # [#...], this becomes the default initial value for all variables, but subsequent items (re)set the initial value for variables in subsequent *varlists*. If the df for a variable in the model is d > 1 then ##... consists of d/2 items. Typically d = 2 so that there is just one initial value, #.

iter(#) sets # to be the maximum number of iterations allowed for the fitting algorithm to converge. The default is 100.

ltolerance(#) is the maximum difference in deviance between iterations required for convergence of the fitting algorithm. The default is 0.001. powers (numlist) defines the powers to be used with fractional polynomial initialization for xvarlist.

trace reports the progress of the fitting procedure towards convergence.

zero (varlist) transforms negative and zero values of all members of varlist (a subset of xvarlist) to zero before fitting the model.

Fitted values, standard errors, graphs

Fitted values and standard errors from a Box-Tidwell model may be obtained by using Stata's fracpred command. The fitted functions for each predictor may be plotted using Stata's fracplot command.

Note

Please ensure that you have a release or update of Stata 6 no earlier than 4 March 1999. The update of 4 March 1999 contains some important changes to fracpoly which affect boxtid.

Acknowledgment

The research received financial support from project grant number 045512/Z/95/Z from The Wellcome Trust.

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ssa13	Analysis of multiple failure-time data with Stata
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1. Introduction

Multiple failure-time data or multivariate survival data are frequently encountered in biomedical and other investigations. These data arise from time-to-occurrence studies when either of two or more events (failures) occur for the same subject, or from identical events occurring to related subjects such as family members or classmates. In these studies, failure times are correlated within cluster (subject or group), violating the independence of failure times assumption required in traditional survival analysis.

In this paper we follow Therneau's (1997) suggestion that for analyses purposes, failure events be classified according to (1) whether they have a natural order, and (2) whether they are recurrences of the same types of events. Failures of the same type include, for example, repeated lung infections with pseudomonas in children with cystic fibrosis, or the development of breast cancer in genetically predisposed families. Failures of different types include adverse reactions to therapy in cancer patients on a particular treatment protocol, or the development of connective tissue disease symptoms in a group of third graders exposed to hazardous waste.

Ordered events may result from a study that records the time to first myocardial infarction (MI), second MI, and so on. These are ordered events in the sense that the second event can not occur before the first event. Unordered events, on the other hand, can occur in any sequence. For example, in a study of liver disease patients, a panel of 7 liver function laboratory tests can become abnormal in a specific order for one patient and in different order for another patient. The order in which the tests become abnormal (fail) is random.

The simplest way of analyzing multiple failure data is to examine time to first event, ignoring additional failures. This approach, however, is usually not adequate because it wastes possibly relevant information. Alternative methods have been developed that make use of all available data while accounting for the lack of independence of the failure times. Two approaches to modeling these data have gained popularity over the last few years. In the first approach, the frailty model method, the association between failure times is explicitly modeled as a random-effect term, called the frailty. Frailties are unobserved effects shared by all members of the cluster. These unmeasured effects are assumed to follow a known statistical distribution, often the gamma distribution, with mean equal to one and unknown variance. This paper will not consider frailty models further.

In the second approach, the dependencies between failure times are not included in the models. Instead, the covariance matrix of the estimators is adjusted to account for the additional correlation. These models, which we will call "variance-corrected"

models, are easily estimated in Stata. In this paper we illustrate the principal ideas and procedures for estimating these models using the Cox proportional hazard model. There is no theoretical reason, however, why other hazard functions could not be used.

2. Methods

Let X_{ki} and C_{ki} be the failure and censoring time of the k^{th} failure type (k = 1, ..., K) in the i^{th} cluster (i = 1, ..., m), and let Z_{ki} be a p-vector of possibly time-dependent covariates, for i^{th} cluster with respect to the k^{th} failure type. "Failure type" is used here to mean both failures of different types, and failures of the same type. Assume that X_{ki} and C_{ki} are independent, conditional on the covariate vector (Z_{ki}) . Define $T_{ki} = \min(X_{ki}, C_{ki})$ and $\delta_{ki} = I(X_{ki} \leq C_{ki})$ where I(.) is the indicator function, and let β be a p-vector of unknown regression coefficients. Under the proportional hazard assumption, the hazard function of the i^{th} cluster for the k^{th} failure type is

$$\lambda_k(t; Z_{ki}) = \lambda_0(t) e^{Z_{ki}\beta} \tag{1}$$

if the baseline hazard function is assumed to be equal for every failure type, or

$$\lambda_k(t; Z_{ki}) = \lambda_{0k}(t) e^{Z_{ki}\beta} \tag{2}$$

if the baseline hazard function is allowed to differ by failure type (Lin 1994).

Maximum likelihood estimates of β for models (1) or (2) are obtained from the Cox's partial likelihood function, $L(\beta)$, assuming independence of failure times. The estimator $\hat{\beta}$ has been shown to be a consistent estimator for β and asymptotically normal as long as the marginal models are correctly specified (Lin 1994). The resulting estimated covariance matrix obtained as the inverse of the information matrix, however,

$$I^{-1} = -\partial^2 \log L(\beta) / \partial \beta \partial \beta'$$

does not take into account the additional correlation in the data, and therefore, it is not appropriate for testing or constructing confidence intervals for multiple failure time data.

Lin and Wei (1989) proposed a modification to this naive estimate, appropriate when the Cox model is misspecified. The resulting robust variance-covariance matrix is estimated as

$$V = I^{-1}U'UI^{-1}$$

where U is a $n \ge p$ matrix of efficient score residuals. The above formula assumes that the n observations are independent. When observations are not independent, but can be divided into m independent groups $(G_1, G_2, ..., G_m)$, then the robust covariance matrix takes the form

$$V = I^{-1}G'GI^{-1}$$

where G is a $m \ge p$ matrix of the group efficient score residuals. In terms of Stata, V is calculated according to the first formula when the robust option is specified and according to the second formula when cluster() is also specified. (cluster() implies robust in Stata, so specifying cluster() by itself is adequate).

3. Implementation and examples

All variance-adjusted models suggested to date can be estimated in Stata. All that is required is some preliminary thought about the analytic model required, the correct way to set up the data, and the command options to be specified.

The examples in this section are presented under the following headings

Unordered failure events Unordered failure events of the same type Unordered failure events of different types (competing risk) Ordered failure events The Andersen–Gill model The marginal risk set model The conditional risk set model (time from entry) The conditional risk set model (time from the previous event)

All the examples we will described use the survival time (st) system, which is to say, for instance, in terms of stcox rather than cox. Although it is not necessary that the st system be used, it is recommended.

The steps for analyzing multiple failure data in Stata are (1) decide whether the failure events are ordered or unordered, (2) select the proper statistical model for the data, (3) organize the data according to the model selected, and (4) use the proper commands and command options to stset the data and estimate the model. Much of this paper deals with the appropriate method for setting the data and the correct way of specifying the estimation command. The examples are used solely to illustrate these processes. Consult the references for more detail discussions on these methods and the datasets used.

3.1 Unordered failure events

The data setup for the analysis of unordered events is relatively simple. One first decides if the failure events are of the same type or of different type, or equivalently, whether the baseline hazard should be equal for all event types or should be allowed to vary by event type. Failure events of the same type are described in section 3.1.1. In section 3.1.2, the baseline hazard is allowed to vary by failure type and is used to examine a competing-risk dataset.

3.1.1 Unordered failure events of the same type

A possible source of correlated failure times of the same event type are familial studies, in which each family member is at risk of developing a disease of interest. Failure times of family members are correlated because they share genetic and perhaps environmental factors.

Another source of correlated failure times of the same type are studies where the same event can occur on the same individual multiple times. This is rare because we are also restricting the events to have no order. Lee, Wei, and Amato (1992) analyzed data from the National Eye Institute study on the efficacy of photocoagulation as a treatment for diabetic retinopathy. In that study, each subject was treated with photocoagulation on one randomly selected eye while the other eye served as an untreated matched control. The outcome of interest was the onset of severe visual loss, and the study hoped to show that laser photocoagulation significantly reduced the time to onset of blindness. In this study, the sampling units, the eyes, are pairwise correlated, the failure types are the same, and unordered because the right eye can fail before the left eye or vice versa.

These types of data are straightforward to setup and analyze in Stata. Each sampling unit is entered once into the dataset. In the family data, each family member appears as an observation in the dataset and an id variable identifies his or her family. In the laser photocoagulation example, because each eye is a sampling unit, each eye appears as an observation in the dataset. Therefore, if there are n patients in the diabetic retinopathy study then the resulting dataset would contain 2n observations. A variable is used to identify the matched eyes.

We will illustrate using a subset of the diabetic retinopathy data. The data from 197 high-risk patients was entered into a Stata dataset. The first four observations are

list	in 1/4, noobs			
id	time	cens	agegrp	treat
5	46.23	0	1	1
5	46.23	0	1	0
14	42.5	0	0	1
14	31.3	1	0	0

Each patient has two observations in the dataset, one for the treated eye (treat==1) and another for the "control" eye, treat==0. The data, therefore, contain 394 observations. Each eye is assumed to enter the study at time 0 and it is followed until blindness develops or censoring occurs. The follow-up time is given by the variable time. The four observations listed above correspond to patients with id=5 and id=14.

After creating the dataset, it is then stset as usual, however the id() option is not specified. Specifying id() would cause stset to interpret subjects with the same id() as the same sampling unit and would drop them because of overlapping study times. Thus, we type

Note that stset correctly reports that there are 394 observations. The command for estimating the corresponding Cox model is

```
. stcox agegrp treat, cluster(id) efron nohr
Iteration 0: log likelihood = -867.98581
            log likelihood = -856.74901
Iteration 1:
Iteration 2: log likelihood = -856.74456
Refining estimates:
Iteration 0: log likelihood = -856.74456
Cox regression -- Efron method for ties
No. of subjects =
                      394
                                          Number of obs
                                                               394
No. of failures =
                      155
           = 14018.24001
Time at risk
                                           Wald chi2(2)
                                                             27.71
                                                        =
                                                            0.0000
Log likelihood = -856.74456
                                          Prob > chi2
                          (standard errors adjusted for clustering on id)
     _t |
                    Robust
     _d |
             Coef. Std. Err.
                                      P>|z|
                                               [95% Conf. Interval]
                               z
    _____
                  .1790951
.1488857
 agegrp
         .0538829
                               0.301
                                      0.764
                                               -.2971371
                                                         .4049028
  treat -.7789297
                                                          -.487119
                              -5.232 0.000
                                                -1.07074
               _____
```

The cluster(id) option specifies to stcox which observations are related. Stata knows to produce robust standard errors whenever the cluster() option is used. The efron option requests that Efron's method for handling ties be used and the nohr option is used to request that coefficients, instead of hazard ratios, be reported.

3.1.2 Unordered failure events of different types (competing risk)

A common data source of unordered failure events of different types are competing-risk studies. In these studies, a patient can suffer several outcomes of interest in random order. In the analysis of these data, the baseline hazard function is allowed to vary by failure type. This is accomplished by stratifying the data on failure type, allowing each stratum to have its own baseline hazard function, but restricting the coefficients to be the same across strata.

We illustrate the use of Stata in the analysis of a competing-risk model, with a subset of the Mayo Clinic's Ursodeoxycholic acid (UDCA) data (Lindor et al. 1994). The data consists of 170 patients with primary biliary cirrhosis randomly allocated to either the UDCA treatment group or a group receiving a placebo. The times up to nine possible events were recorded: death, liver transplant, voluntary withdraw, histologic progression, development of varices, development of ascites, development of encephalophathy, doubling of bilirubin, and worsening of symptoms. All times were measured from the date of treatment allocation.

An important characteristic of these failure events is that each can occur only once per subject. Note that all subjects are at risk for all events, and also, that when a subject experiences one of the events, he remains at risk for all other events. Therefore, if there are k possible events, each subject will appear k times in the dataset, once for each possible failure. Here is the resulting data for two of the subjects.

. list id rx bili time status rec if id==5 | id==18,nod noobs

id	rx	bili	time	status	rec
5	placebo	.0953102	1875	0	1
5	placebo	.0953102	1875	0	2
5	placebo	.0953102	1875	0	3
5	placebo	.0953102	1875	0	4
5	placebo	.0953102	1875	0	5
5	placebo	.0953102	1875	0	6

5	placebo	.0953102	1875	0	- 7
5	placebo	.0953102	1875	0	8
5	placebo	.0953102	1875	0	9
18	placebo	.1823216	391	1	9
18	placebo	.1823216	391	1	8
18	placebo	.1823216	763	1	5
18	placebo	.1823216	765	0	2
18	placebo	.1823216	765	0	1
18	placebo	.1823216	765	0	6
18	placebo	.1823216	765	0	7
18	placebo	.1823216	765	1	3
18	placebo	.1823216	765	0	4

Each patient appears nine times, once for each possible event. The event type, rec, is coded as 1 through 9. Patient number 5, did not experience any events during the 1,875 days of follow-up. Thus, he appears censored nine times in the data, each observation recording the complete follow-up period. Patient 18 experienced 4 events: rec=8 (doubling of bilirubin), rec=9 (worsening of symptoms), rec=5 (development of varices) and rec=3 (voluntary withdraw).

The command to stset the data is used without specifying the id() option.

```
. stset time, failure(status)
   failure event: status ~= 0 & status ~= .
obs. time interval: (0, time]
exit on or before: failure
_____
   1530 total obs.
    0 exclusions
_____
   1530 obs. remaining, representing
    145 failures in single record/single failure data
 1808720 total analysis time at risk, at risk from t =
                                              0
                    earliest observed entry t =
                                              0
                                            1896
                        last observed exit t =
```

It correctly reported 1,530 observations (170x9).

The id variable will be used to cluster the related observations when estimating the Cox model. Additionally, it does not seem reasonable to assume that each failure type should have the same baseline hazard, thus the Cox model will be stratified by failure type.

. stcox r	x bili hi_sta	, nohr efron	robust st	rata(rec)	cluster(id)	nolo	g
Stratified	d Cox regr	- Efron metho	d for ties	3			
No. of sul	bjects =	1530		Nu	mber of obs	=	1530
No. of fa:	ilures =	145					
Time at r:	isk =	1808720					
				Wa	ld chi2(3)	=	31.99
Log likel:	ihood = -66	62.44704		Pr	ob > chi2	-	0.0000
		(sta	ndard erro	ors adjus	ted for clus	terin	g on id)
_t	l	Robust					
_d	Coef.	Std. Err.	z	P> z	[95% Co	onf. I	nterval]
rx	9371209	.240996	-3.889	0.000	-1.40946	 64 -	.4647774
bili	.5859002	.1491832	3.927	0.000	.293506	35	.8782939
hi_stage	0754988	.2777845	-0.272	0.786	619946	64	.4689488
					Stra	tifie	d by rec

The covariates are treatment group (rx), log(bilirubin)(bili), and high histologic stage indicator (hi_stage).

3.2 Ordered failure events

There are several approaches to the analysis of ordered events. The principal difference between these methods is in the way that the risk sets are defined at each failure time. The simplest method to implement in Stata follows the counting process approach of Andersen and Gill (1982). The basic assumption is that all failure types are equal or indistinguishable. The problem then reduces to the analysis of time to first event, time to second event, and so on. Thus, the risk set at time t for event k, is all subjects under observation at time t. A major limitation of this approach is that it does not allow more than one event to occur at a given time. For example, in a study examining time to side effects of a new medication, if a patient exhibits two

side effects at the same time, the corresponding observations are dropped because the time span between failures is zero. This approach is illustrated in section 3.2.1.

A second model, proposed by Wei, Lin, and Weissfeld (1989), is based on the idea of marginal risk sets. For this analysis, the data is treated like a competing risk dataset, as if the failure events were unordered, so each event has its own stratum and each patient appears in all strata. The marginal risk set at time t for event k, is made up of all subjects under observation at time t that have not had event k. This approach is illustrated in section 3.2.2.

A third method proposed by Prentice, Williams, and Peterson (1981) is known as the conditional risk set model. The data is setup as for Andersen and Gill's counting processes method, except that the analysis is stratified by failure order. The assumption made is that a subject is not at risk of a second event until the first event has occurred and so on. Thus the conditional risk set at time t for event k, is made up of all subjects under observation at time t, that have had event k - 1. There are two variations to this approach. In the first variation, time to each event is measured from entry time, and in the second variation, time to each event is measured from the previous event. This approach is illustrated in sections 3.2.3 and 3.2.4.

The above three approaches will be illustrated using the bladder cancer data presented by Wei, Lin, and Weissfeld (1989). These data were collected from a study of 85 subjects randomly assigned to either a treatment group receiving the drug thiotepa or to a group receiving a placebo control. For each patient, time for up to four tumor recurrences was recorded in months (r1 - r4). These are the first nine observations in the data.

. list in 1/9,noobs nod

id	group	futime	number	size	r1	r2	r3	r4
1	placebo	1	1	3	0	0	0	0
2	placebo	4	2	1	0	0	0	0
3	placebo	7	1	1	0	0	0	0
4	placebo	10	5	1	0	0	0	0
5	placebo	10	4	1	6	0	0	0
6	placebo	14	1	1	0	0	0	0
7	placebo	18	1	1	0	0	0	0
8	placebo	18	1	3	5	0	0	0
9	placebo	18	1	1	12	16	0	0

The id variable identifies the patients, group is the treatment group, futime is the total follow-up time for the patient, number is the number of initial tumors, size is the initial tumor size, and r1 to r4 are the times to first, second, third, and fourth recurrence of tumors. A recurrence time of zero indicates no tumor.

3.2.1 The Andersen–Gill model

To implement the Andersen and Gill model using the results from the bladder cancer study, the data are set up as follows: for each patient there must be one observation per event or time interval. For example, if a subject has one event, then there will be two observations for that subject. The first observation will cover the time span from entry into the study until the time of the event, and the second observation spans the time from the event to the end of follow-up. The data for the nine subjects listed above is

. list if id<10, noobs nod

id	group	time0	time	status	number	size
1	placebo	0	1	0	1	3
2	placebo	0	4	0	2	1
3	placebo	0	7	0	1	1
4	placebo	0	10	0	5	1
5	placebo	0	6	1	4	1
5	placebo	6	10	0	4	1
6	placebo	0	14	0	1	1
7	placebo	0	18	0	1	1
8	placebo	0	5	1	1	3
8	placebo	5	18	0	1	3
9	placebo	0	12	1	1	1
9	placebo	12	16	1	1	1
9	placebo	16	18	0	1	1

In the original data, subjects 1 through 4 had no tumors recur, thus, each of these 4 patients has only one censored (status=0) observation spanning from time0=0 to end of follow-up (time=futime). Patient 5 (id=5) had one tumor recur at 6 months and was followed until month 14. This patient has two observations in the final dataset; one from time0=0 to tumor recurrence (time=6), ending in an event (status=1), and another from time0=6 to end of follow-up (time=10), ending as censored (status =0).

We stset the data with the command

```
. stset time, fail (status) exit(futime) id(id) enter(time0)
               id: id
     failure event: status ~= 0 & status ~= .
obs. time interval: (time[_n-1], time]
 enter on or after: time time0
 exit on or before: time futime
     178 total obs.
      0 exclusions
     178 obs. remaining, representing
      85 subjects
     112 failures in multiple failure-per-subject data
     2480 total analysis time at risk, at risk from t =
                                                               0
                            earliest observed entry t =
                                                               0
                                 last observed exit t =
                                                              59
```

and we estimate the Andersen-and-Gill Cox model as

. stcox group size number, nohr efron robust nolog Cox regression -- Efron method for ties No. of subjects = 85 178 Number of obs = 112 No. of failures = Time at risk 2480 Wald chi2(3) = 11.41 Prob > chi2 Log likelihood = -449.98064 = 0.0097 (standard errors adjusted for clustering on id) _____ _t | Robust _d Coef. Std. Err. P>|z| [95% Conf. Interval] z group | -.464687 .2671369 -1.740 0.082 size | -.0436603 .0780767 -0.559 0.576 -.9882656 .0588917 .0780767 -.1966879 .1093673 number .1749604 .0634147 2.759 0.006 .0506699 .2992509

This time it was necessary to specify the cluster() option. Because stset's id() option was used, Stata knows to cluster on the id() variable when producing robust standard errors.

3.2.2 The marginal risk set model (Wei, Lin, and Weissfeld)

The setup for the marginal risk model is identical to the competing risk model described in section 3.1.2. In essence the model ignores the ordering of events and treats each failure occurrence as belonging in an independent stratum.

The resulting data for the first six of the nine subjects listed above are

. list id	group time	status numbe	r size	rec if id<7,	noobs nod	
id	group	time	status	number	size	rec
1	placebo	1	0	1	3	1
1	placebo	1	0	1	3	2
1	placebo	1	0	1	3	3
1	placebo	1	0	1	3	4
2	placebo	4	0	2	1	1
2	placebo	4	0	2	1	2
2	placebo	4	0	2	1	3
2	placebo	4	0	2	1	4
3	placebo	7	0	1	1	1
3	placebo	7	0	1	1	2
3	placebo	7	0	1	1	3
3	placebo	7	0	1	1	4
4	placebo	10	0	5	1	1
4	placebo	10	0	5	1	2
4	placebo	10	0	5	1	3
4	placebo	10	0	5	1	4
5	placebo	6	1	4	1	1
5	placebo	10	0	4	1	2
5	placebo	10	0	4	1	3
5	placebo	10	0	4	1	4
6	placebo	14	0	1	1	1
6	placebo	14	0	1	1	2
6	placebo	14	0	1	1	3
6	placebo	14	0	1	1	4

The data is then stset without specifying the id() option

and the Cox model is estimated by clustering on id and stratifying on the failure occurrence variable (rec).

```
. stcox group size number, nohr efron strata(rec) cluster(id) nolog
Stratified Cox regr. -- Efron method for ties
No. of subjects = 340
                                        Number of obs =
                                                           340
No. of failures = 112
Time at risk
           = 8522
                                        Wald chi2(3)
                                                         15.35
Log likelihood = -426.14683
                                       Prob > chi2
                                                    =
                                                         0.0015
                        (standard errors adjusted for clustering on id)
   _____
    _t |
                   Robust
    _d |
            Coef. Std. Err.
                              z
                                   P> z
                                            [95% Conf. Interval]
 group | -.5847935 .3097738 -1.888 0.059
                                                      .0223521
                                            -1.191939
                 .095148 -0.542 0.587
.0670372 3.137 0.002
                                                      .1348697
  size -.051617
                                           -.2381036
 number .2102937
                                            .0789032
                                                     .3416842
          _____
                  _____
                                            _____
```

Stratified by rec

3.2.3 The conditional risk set model (time from entry)

As previously mentioned, there are two variations of the conditional risk set model. The first variation in which time to each event is measured from entry is illustrated in this section.

The data is set up as for Andersen and Gill's method, however, a variable indicating the failure order is included.

The resulting observations for the first nine subjects are

. list	id if id<10	,noobs nod					
id	group	timeO	time	status	number	size	str
1	placebo	0	1	0	1	3	1
2	placebo	0	4	0	2	1	1
3	placebo	0	7	0	1	1	1
4	placebo	0	10	0	5	1	1
5	placebo	0	6	1	4	1	1
5	placebo	6	10	0	4	1	2
6	placebo	0	14	0	1	1	1
7	placebo	0	18	0	1	1	1
8	placebo	0	5	1	1	3	1
8	placebo	5	18	0	1	3	2
9	placebo	0	12	1	1	1	1
9	placebo	12	16	1	1	1	2
9	placebo	16	18	0	1	1	3

The resulting dataset is identical to that used to fit Andersen and Gill's model except that the str variable identifies the failure risk group for each time span. For the first 4 individuals, who have not had a tumor recur, the str value is one, meaning that during their total observed time they are at risk of first failure. The last individual listed, id=9, was at risk of a first recurrence for 12 months (str=1), at risk of a second recurrence from 12 through 16 months (str=2), and at risk of a third recurrence from 16 months to the end of follow-up (str=3).

The stset command is identical to that used for the Andersen and Gill model.

```
. stset time, fail (status) exit(futime) id(id) enter(time0)
            id: id
   failure event: status ~= 0 & status ~= .
obs. time interval: (time[_n-1], time]
enter on or after: time time0
exit on or before: time futime
_____
    178 total obs.
     0 exclusions
_____
                 _____
    178 obs. remaining, representing
     85 subjects
    112 failures in multiple failure-per-subject data
   2480 total analysis time at risk, at risk from t =
                                                 0
                                                 0
                     earliest observed entry t =
                         last observed exit t =
                                                59
```

The corresponding conditional risk model is

. stcox group size number,nohr efron robust nolog strata(strata)

Stratified	l Cox regr	- Efron meth	od for ties	5			
No. of sub	jects =	85		N	umber of obs	=	178
No. of fai	ilures =	112					
Time at ri	isk =	2480					
				Wa	ald chi2(3)	=	7.17
Log likelihood = -315.99082 Prob > chi2 = 0.0665							0.0665
		(st	andard erre	ors adju	sted for clus	teri	ng on id)
_t		Robust					
_d	Coef.	Std. Err.	z	P> z	[95% Cc	nf.	Interval]
group	3334887	.2060021	-1.619	0.105	737245	5	.070268
size	0084947	.062001	-0.137	0.891	130014	4	.1130251
number	.1196172	.0516917	2.314	0.021	.018303	3	.2209311
					Stratif	ied	by strata

3.2.4 The conditional risk set model (time from the previous event)

The second variations of the conditional risk set model, measures time to each event from the time of the previous event.

The data is set up as in 3.2.3, except that time is not measured continuously from study entry, but the clock is set to zero after each failure.

. list id	if id<10,noo	bs nod					
id	group	timeO	time	status	number	size	str
1	placebo	0	1	0	1	3	1
2	placebo	0	4	0	2	1	1
3	placebo	0	7	0	1	1	1
4	placebo	0	10	0	5	1	1
5	placebo	0	4	0	4	1	2
5	placebo	0	6	1	4	1	1
6	placebo	0	14	0	1	1	1
7	placebo	0	18	0	1	1	1
8	placebo	0	5	1	1	3	1
8	placebo	0	13	0	1	3	2
9	placebo	0	2	0	1	1	3
9	placebo	0	4	1	1	1	2
9	placebo	0	12	1	1	1	1

Note that the initial times for all time spans are set to zero and that the time variable now reflects the length of the time span. After creating the new time variable, the data needs to be stset again.

. stset time,fail(status) exit(futime) enter(time0)
 failure event: status ~= 0 & status ~= .
obs. time interval: (0, time]
enter on or after: time time0
exit on or before: time futime

178 total obs. 0 exclusions 178 obs. remaining, representing 112 failures in single record/single failure data 2480 total analysis time at risk, at risk from t = 0 earliest observed entry t = 0 last observed exit t = 59

The corresponding conditional risk model is

. stcox gr	oup size numb	ber,nohr efro	n robust 1	nolog stra	ta(str) clu	ster(id)
Stratified	l Cox regr	- Efron metho	d for ties	3		
No. of sub	jects =	178		Num	ber of obs	= 178
No. of fai	lures =	112				
Time at ri	.sk =	2480				
				Wal	d chi2(3)	= 11.70
Log likeli	.hood = -38	58.96849		Pro	b > chi2	= 0.0085
		(sta	ndard erro	ors adjust	ed for clust	tering on id)
_t		Robust				
_d	Coef.	Std. Err.	z	P> z	[95% Con	nf. Interval]
group	2790045	.2169035	-1.286	0.198	704127	.1461186
size	.0074151	.0647143	0.115	0.909	1194220	.1342528
number	.1580459	.0512421	3.084	0.002	.0576133	.2584785

Stratified by strata

4. Conclusion

This paper details how Stata can be used to fit variance-corrected models for the analysis of multiple failure-time data. The examples used to illustrate the various approaches, although real, were simple. More complicated datasets, however, containing time-dependent covariates, varying time scales, delayed entry and other complications, can be set up and analyzed following the guidelines illustrated in this paper.

The most important aspect in the implementation of the methods described, is the accurate construction of the dataset for analysis. Care must be taken to correctly code entry and exit times, strata variables and failure/censoring indicators. It is strongly recommended that, after creating the final dataset and before analyzing and reporting results, the data be examined thoroughly. Lists of all representative, and especially complex cases, should be carefully verified. This step, although time consuming and tedious, is indispensable, especially when working with complicated survival data structures.

A second important aspect of the analysis, is the proper use of the stset command. Become familiar and have a clear understanding of the id(), origin(), enter() and timeO() options. Review the output from stset and confirm that the final data contains the expected number of observations and failures. Check any records dropped and verify the data, especially the stset created variables, by listing and examining observations.

Lastly fit the model using the correct stcox options to produce robust standard errors and, if needed, the strata specific baseline hazard.

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STB-49

zz9	Cumulative Index for STB-43–STB-48
220	

[an] Announcements

STB-43	2	an66	STB-37–STB-42 available in bound format
STB-47	2	an67	Stata 5, Stata 6, and the STB
STB-47	2	an68	NetCourse schedule announced

[dm] Data Management

STB-43	2	dm55	Generating sequences and patterns of numeric data: an extension to egen
STB-43	3	dm56	A labels editor for Windows and Macintosh
STB-43	6	dm57	A notes editor for Windows and Macintosh
STB-43	9	dm58	A package for the analysis of (husband-wife) data
STB-44	2	dm59	Collapsing datasets to frequencies
STB-45	2	dm60	Digamma and trigamma functions
STB-45	2	dm61	A tool for exploring Stata datasets (Windows and Macintosh only)
STB-45	5	dm62	Joining episodes in multi-record survival time data
STB-46	2	dm63	Dialog box window for browsing, editing, and entering observations
STB-46	6	dm64	Quantiles of the studentized range distribution

[gr] Graphics

STB-45	6	gr29	labgraph: placing text labels on two-way graphs
STB-46	10	gr29.1	Correction to labgraph
STB-45	7	gr30	A set of 3D-programs
STB-45	14	gr31	Graphical representation of follow-up by time bands
STB-46	10	gr32	Confidence ellipses
STB-46	13	gr33	Violin plots
STB-47	3	gr34	Drawing Venn diagrams
STB-48	2	gr34.1	Drawing Venn diagrams
STB-48	2	gr35	Diagnostic plots for assessing Singh-Maddala and Dagum distributions fitted by MLE

[ip] Instruction on Programming

STB-45	17	ip14.1	Programming utility: numeric lists (correction and extension)
STB-43	13	ip25	Parameterized Monte Carlo simulations: an enhancement to the simulation command
STB-45	17	ip26	Bivariate results for each pair of variables in a list
STB-45	20	ip27	Results for all possible combinations of arguments

[sbe] Biostatistics & Epidemiology

STB-43	15	sbe16.2	Corrections to the meta-analysis command
STB-45	21	sbe18.1	Update of sampsi
STB-44	3	sbe19.1	Tests for publication bias in meta-analysis
STB-44	4	sbe24	metan-an alternative meta-analysis command
STB-45	21	sbe24.1	Correction to funnel plot
STB-47	8	sbe25	Two methods for assessing the goodness-of-fit of age-specific reference intervals
STB-47	15	sbe26	Assessing the influence of a single study in the meta-analysis estimate

[sg] General Statistics

STB-43	16	sg33.1	Enhancements for calculation of adjusted means and adjusted proportions
STB-43	24	sg81	Multivariable fractional polynomials
STB-43	32	sg82	Fractional polynomials for st data
STB-43	32	sg83	Parameter estimation for the Gumbel distribution
STB-43	35	sg84	Concordance correlation coefficient
STB-45	21	sg84.1	Concordance correlation coefficient, revisited
STB-44	15	sg85	Moving summaries
STB-44	18	sg86	Continuation-ratio models for ordinal response data
STB-44	22	sg87	Windmeijer's goodness-of-fit test for logistic regression
STB-44	27	sg88	Estimating generalized ordered logit models
STB-44	30	sg89	Adjusted predictions and probabilities after estimation
STB-45	23	sg89.1	Correction to the adjust command

STB-46	18	sg89.2	Correction to the adjust command
STB-45	23	sg90	Akaike's information criterion and Schwarz's criterion
STB-45	26	sg91	Robust variance estimators for MLE Poisson and negative binomial regression
STB-45	28	sg92	Logistic regression for data including multiple imputations
STB-45	30	sg93	Switching regressions
STB-46	18	sg94	Right, left, and uncensored Poisson regression
STB-46	20	sg95	Geographically weighted regression: A method for exploring spatial nonstationarity
STB-46	24	sg96	Zero-inflated Poisson and negative binomial regression models
STB-46	28	sg97	Formatting regression output for published tables
STB-46	30	sg98	Poisson regression with a random effect
STB-47	17	sg99	Multiple regression with missing observations for some variables
STB-47	24	sg100	Two-stage linear constrained estimation
STB-47	31	sg101	Pairwise comparisons of means, including the Tukey wsd method
STB-47	37	sg102	Zero-truncated Poisson and negative binomial regression
STB-47	40	sg103	Within subjects (repeated measures) ANOVA, including between subjects factors
STB-48	4	sg104	Analysis of income distributions
STB-48	18	sg105	Creation of bivariate random lognormal variables
STB-48	19	sg106	Fitting Singh-Maddala and Dagum distributions by maximum likelihood
STB-48	25	sg107	Generalized Lorenz curves and related graphs
STB-48	29	sg108	Computing poverty indices
STB-48	33	sg109	Utility to convert binomial frequency records to frequency weighted data
STB-48	34	sg110	Hardy-Weinberg equilibrium test and allele frequency estimation

[ssa] Survival Analysis

STB-44 37 ssa12 Predicted survival curves for the Cox proportional hazards model

[svy] Survey Sample

STB-45 33 svy7 Two-way contingency tables for survey or clustered data

[sts] Time-series, Econometrics

STB-46 33 sts13 Time series regression for counts allowing for autocorrelation

[zz] Not elsewhere classified

STB-43 39 zz8 Cumulative index for STB-37–STB-42

STB categories and insert codes

Inserts in the STB are presently categorized as follows:

Gene	ral Categories:		
an	announcements	ip	instruction on programming
сс	communications & letters	OS	operating system, hardware, &
dm	data management		interprogram communication
dt	datasets	qs	questions and suggestions
gr	graphics	tt	teaching
in	instruction	ZZ	not elsewhere classified
Statis	stical Categories:		
sbe	biostatistics & epidemiology	ssa	survival analysis
sed	exploratory data analysis	ssi	simulation & random numbers
sg	general statistics	SSS	social science & psychometrics
smv	multivariate analysis	sts	time-series, econometrics
snp	nonparametric methods	svy	survey sampling
sqc	quality control	sxd	experimental design
sqv	analysis of qualitative variables	SZZ	not elsewhere classified
srd	robust methods & statistical diagnostics		

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Articles include new Stata commands (ado-files), programming tutorials, illustrations of data analysis techniques, discussions on teaching statistics, debates on appropriate statistical techniques, reports on other programs, and interesting datasets, announcements, questions, and suggestions.

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- 2. Any ado-files, .exe files, or other software that accompanies the submission.
- 3. A help file for each ado-file included in the submission. See any recent STB diskette for the structure a help file. If you have questions, fill in as much of the information as possible and we will take care of the details.
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- 5. Files containing the graphs to be included in the insert. If you have used STAGE to edit the graphs in your submission, be sure to include the .gph files. Do not add titles (e.g., "Figure 1: ...") to your graphs as we will have to strip them off.

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