stintreg — Parametric models for interval-censored survival-time data

DescriptionQuick startOptionsRemarks and examplesReferencesAlso see

Menu Stored results Syntax Methods and formulas

Description

stintreg fits parametric models to survival-time data or, more precisely, event-time data that can be uncensored, right-censored, left-censored, or interval-censored. These models are generalizations of the models fit by streg to support interval-censored data. The supported survival models are exponential, Weibull, Gompertz, lognormal, loglogistic, and generalized gamma. Proportional-hazards (PH) and accelerated failure-time (AFT) parameterizations are provided.

With interval-censored data, the event-time variables are specified with the stintreg command instead of using stset. Any st settings are ignored by stintreg.

Quick start

Weibull survival model with covariates x1 and x2 fit to interval-censored event-time data with lower and upper endpoints t1 and t2

stintreg x1 x2, interval(t1 t2) distribution(weibull)

Use AFT metric instead of PH metric

stintreg x1 x2, interval(t1 t2) distribution(weibull) time

Different intercepts and ancillary parameters for strata identified by svar

stintreg x1 x2, interval(t1 t2) distribution(weibull) strata(svar)

Lognormal survival model

stintreg x1 x2, interval(t1 t2) distribution(lognormal)

Same as above, but also model the logarithm of ancillary parameter as the linear combination of covariates z1 and z2

```
stintreg x1 x2, interval(t1 t2) distribution(lognormal) ///
ancillary(z1 z2)
```

Menu

Statistics > Survival analysis > Regression models > Interval-censored parametric survival models

Syntax

stintreg [*indepvars*] [*if*] [*in*] [*weight*], <u>interval</u>($t_l t_u$) <u>distribution</u>(*distname*)

[options]

options	Description
Model	
* <u>int</u> erval($t_l t_u$)	lower and upper endpoints for the event-time interval
<u>nocons</u> tant	suppress constant term
* <u>dist</u> ribution(<i>distname</i>)	specify survival distribution
time	use accelerated failure-time metric
Model 2	
strata(<i>varname</i>)	strata ID variable
<u>off</u> set(<i>varname</i>)	include varname in model with coefficient constrained to 1
<u>anc</u> illary(<i>varlist</i>)	use varlist to model the first ancillary parameter
anc2(<i>varlist</i>)	use varlist to model the second ancillary parameter
<u>const</u> raints(<i>constraints</i>)	apply specified linear constraints
<pre>epsilon(#)</pre>	tolerance to treat observations as uncensored; default is epsilon(1e-6)
SE/Robust	
vce(<i>vcetype</i>)	<pre>vcetype may be oim, robust, cluster clustvar, opg, bootstrap, or jackknife</pre>
Reporting	
<u>l</u> evel(#)	set confidence level; default is level(95)
nohr	do not report hazard ratios
<u>tr</u> atio	report time ratios
<u>nohead</u> er	suppress header from coefficient table
<u>nocnsr</u> eport	do not display constraints
display_options	control columns and column formats, row spacing, line width, display of omitted variables and base and empty cells, and factor-variable labeling
Maximization	
maximize_options	control the maximization process; seldom used
<u>col</u> linear	keep collinear variables
<u>coefl</u> egend	display legend instead of statistics

*interval(t_l t_u) and distribution(*distname*) are required.

stintreg — Parametric models for interval-censored survival-time data 3

distname	Description
<u>e</u> xponential	exponential survival distribution
gompertz	Gompertz survival distribution
loglogistic	loglogistic survival distribution
<u>ll</u> ogistic	synonym for loglogistic
weibull	Weibull survival distribution
lognormal	lognormal survival distribution
<u>ln</u> ormal	synonym for lognormal
ggamma	generalized gamma survival distribution

varlist may contain factor variables; see [U] 11.4.3 Factor variables.

bootstrap, by, collect, fp, jackknife, nestreg, statsby, stepwise, and svy are allowed; see [U] 11.1.10 Prefix commands.

Weights are not allowed with the bootstrap prefix; see [R] bootstrap.

vce(), noheader, and weights are not allowed with the svy prefix; see $\left[\mathrm{SVY}\right]$ svy.

fweights, iweights, and pweights are allowed; see [U] 11.1.6 weight.

collinear and coeflegend do not appear in the dialog box.

See [U] 20 Estimation and postestimation commands for more capabilities of estimation commands.

Options

Model

 $interval(t_l t_u)$ specifies two time variables that contain the endpoints of the event-time interval. t_l represents the lower endpoint, and t_u represents the upper endpoint. interval() is required.

The interval time variables t_l and t_u should have the following form:

Type of observations		t_l	t_u
uncensored	a = [a, a]	a	a
interval-censored	(a,b]	a	b
left-censored	(0,b]		b
left-censored	(0,b]	0	b
right-censored	$(a,+\infty)$	a	
missing			•
missing		0	

noconstant; see [R] Estimation options.

distribution(distname) specifies the survival model to be fit. distribution() is required.

time specifies that the model be fit in the accelerated failure-time metric rather than in the log relativehazard metric or proportional hazards metric. This option is valid only for the exponential and Weibull models, because these are the only models that have both a proportional hazards and an accelerated failure-time parameterization. Regardless of metric, the likelihood function is the same, and models are equally appropriate viewed in either metric; it is just a matter of changing the interpretation. Model 2

- strata(varname) specifies the stratification ID variable. Observations with equal values of the variable are assumed to be in the same stratum. Stratified estimates (with equal coefficients across strata but intercepts and ancillary parameters distinct for each stratum) are then obtained. varname may be a factor variable; see [U] 11.4.3 Factor variables.
- offset(varname); see [R] Estimation options.
- ancillary (*varlist*) specifies that the ancillary parameter for the Weibull, lognormal, Gompertz, and loglogistic distributions and that the first ancillary parameter (σ) of the generalized log-gamma distribution be estimated as a linear combination of *varlist*.

When an ancillary parameter is constrained to be strictly positive, the logarithm of the ancillary parameter is modeled as a linear combination of *varlist*.

anc2(*varlist*) specifies that the second ancillary parameter (κ) for the generalized log-gamma distribution be estimated as a linear combination of *varlist*.

constraints (*constraints*); see [R] Estimation options.

epsilon(#) specifies that observations with $t_u - t_l < \#$ be treated as uncensored. The default is epsilon(1e-6).

SE/Robust

vce(vcetype) specifies the type of standard error reported, which includes types that are derived from asymptotic theory (oim, opg), that are robust to some kinds of misspecification (robust), that allow for intragroup correlation (cluster clustvar), and that use bootstrap or jackknife methods (bootstrap, jackknife); see [R] vce_option.

Reporting

level(#); see [R] Estimation options.

nohr, which may be specified at estimation or upon redisplaying results, specifies that coefficients rather than exponentiated coefficients be displayed, that is, that coefficients rather than hazard ratios be displayed. This option affects only how coefficients are displayed, not how they are estimated.

This option is valid only for models with a natural proportional hazards parameterization: exponential, Weibull, and Gompertz. These three models, by default, report hazard ratios (exponentiated coefficients).

tratio specifies that exponentiated coefficients, which are interpreted as time ratios, be displayed. tratio is appropriate only for the loglogistic, lognormal, and generalized gamma models, or for the exponential and Weibull models when fit in the accelerated failure-time metric.

tratio may be specified at estimation or upon replay.

noheader suppresses the output header, either at estimation or upon replay.

nocnsreport; see [R] Estimation options.

```
display_options: noci, nopvalues, noomitted, vsquish, noemptycells, baselevels,
allbaselevels, nofvlabel, fvwrap(#), fvwrapon(style), cformat(%fmt), pformat(%fmt),
sformat(%fmt), and nolstretch; see [R] Estimation options.
```

Maximization

maximize_options: difficult, technique(algorithm_spec), iterate(#), [no]log, trace, gradient, showstep, hessian, showtolerance, tolerance(#), ltolerance(#), nrtolerance(#), nonrtolerance, and from(init_specs); see [R] Maximize. These options are seldom used.

Setting the optimization type to technique(bhhh) resets the default vcetype to vce(opg).

The following options are available with stintreg but are not shown in the dialog box:

collinear, coeflegend; see [R] Estimation options.

Remarks and examples

Remarks are presented under the following headings:

Introduction Types of interval-censoring Case II interval-censored data Case I interval-censored data Parameterization of ancillary parameters Stratified estimation

Introduction

stintreg fits parametric models to survival-time data, which can be uncensored, right-censored, leftcensored, or interval-censored. These models are generalizations of the models fit by streg, because they extend the censoring mechanism beyond right-censoring. In the context of interval-censored data, the term "failure-time" or, more generally, "event-time data" is more appropriate than "survival-time data", so we will use it from now on.

In survival analysis, we find different types of censored data. Among them, right-censored data have been studied extensively and can be analyzed using all of Stata's survival commands, including streg and stcox. Research on interval-censored data has also been popular; see, for example, Finkelstein and Wolfe (1985), Odell, Anderson, and D'Agostino (1992), Rabinowitz, Tsiatis, and Aragon (1995), Huang and Wellner (1997), Lindsey (1998), Lindsey and Ryan (1998), Sun (2006), and Sun and Li (2014). Interval-censoring occurs when the failure time of interest is not exactly observed but is known only to lie within some interval (for example, Kalbfleisch and Prentice 2002). Uncensored, right-censored, and left-censored data are special cases of interval-censored data. In these cases, the interval reduces to a single point, is unbounded on the right, or is bounded by zero on the left.

Interval-censored event-time data arise in many areas including medical, epidemiological, financial, and sociological studies. A study may lead to event-time data with different types of censoring. Consider a medical study that involves periodic follow-ups with patients who had breast cancer. In this case, patients are tested on a regular basis, but the time to the recurrence of the cancer may not be measured exactly. If cancer recurs before the first visit, the observation is called left-censored. If cancer recurs between two visits, the observation is called interval-censored. If there is no recurrence by the last visit, the observation is right-censored. To analyze such data, you may fit parametric survival models using stintreg.

Regardless of the type of censoring, stintreg requires the survival outcome to be stored in the dataset as interval data. That is, two time variables, t_l and t_u , that contain the endpoints of the event-time interval must be specified in the interval() option. If the data are left-censored, the lower endpoint is zero and

may be represented in t_l by either a missing value (.) or zero. If the data are right-censored, the upper endpoint is $+\infty$ and is represented in t_u by a missing value. Uncensored data are represented by the two endpoints that are equal. If $0 < t_l < t_u < \infty$, the data are interval-censored. Truly missing values must be represented by missing values in both t_l and t_u or by a 0 in t_l and a missing value in t_u . Typing stset is unnecessary, and stintreg will ignore any settings of stset for the usual trivariate response variable (t_0, t, d) . stintreg does not support data exhibiting delayed entry, gaps, time-varying covariates, and multiple failures.

Two often-used parametric models for adjusting survivor functions for the effects of covariates are the AFT models and the multiplicative or PH models. The survival models supported by stintreg are exponential, Weibull, Gompertz, lognormal, loglogistic, and generalized gamma. The lognormal, loglogistic, and generalized gamma models are implemented as AFT models. The exponential and Weibull models are implemented as both AFT and PH models, and the Gompertz model is implemented only in the PH metric. See *Remarks and examples* in [ST] **streg** for more details about the supported models and distributions.

Types of interval-censoring

Interval-censoring can occur in different forms, and each form represents one type of interval-censored event-time data. stintreg accommodates two important types of interval-censored data that are commonly used in practice: case II interval-censored data and case I interval-censored data. Case II interval-censored data are also referred to as general interval-censored data, and case I interval-censored data are also referred to as current status data. We describe each censoring type in detail below. Also see Sun (2006) for more information about different types of interval censoring.

Case II interval-censored data

The most general case of interval-censoring is case II interval-censoring. This type of intervalcensoring occurs when we do not know the exact failure time t, but only know that the failure happened within a random time interval $(t_l, t_u]$, or before the right endpoint of the time interval t_u , or after the left endpoint of the time interval t_l . The following is an example of case II interval-censored data, which contain left-, right-, and interval-censored observations.

Example 1: Case II interval-censoring

Sun (2006) presented parametric analysis of a retrospective study of early breast cancer patients, originally from Finkelstein and Wolfe (1985), that compared the cosmetic effects of two cancer treatments: radiotherapy alone versus radiotherapy plus adjuvant chemotherapy. There were 46 radiotherapy-only patients and 48 radiation-plus-chemotherapy patients who were observed every four to six months. Patients had different visit times and durations between visits. At each visit, the physician recorded a measure of breast retraction. The event of interest was breast retraction. Because patients were observed at random follow-up times, the exact time of breast retraction was not observed and was known only to fall in the interval between visits. The data consist of two interval variables, ltime and rtime, that represent the last clinic visit time when breast retraction had not yet occurred and the first clinic visit time when breast retraction was detected.

To study the effect of treatment on breast retraction, we fit a Weibull model of time to breast retraction on treatment treat using stintreg. Unlike streg, in which the survival variables are set using stset and do not appear in the command, the interval variables ltime and rtime are required for stintreg and are specified in the interval() option:

. use https:// (Cosmetic dete	-					
. stintreg i.	treat, interva	al(ltime rti	me) dist	ribution	(weibull)	
Fitting consta Iteration 0: Iteration 1: Iteration 2: Iteration 3: Iteration 4: Iteration 5: Iteration 6: Iteration 7:	ant-only model Log likelihoo Log likelihoo Log likelihoo Log likelihoo Log likelihoo Log likelihoo Log likelihoo Log likelihoo	d = -200.17 $d = -175.09$ $d = -155.03$ $d = -149.07$ $d = -148.7$ $d = -148.65$ $d = -148.65$	443 621 347 602 639 584			
Fitting full r Iteration 0: Iteration 1: Iteration 2: Iteration 3: Iteration 4:	nodel: Log likelihoo Log likelihoo Log likelihoo Log likelihoo Log likelihoo	d = -143.53 d = -143.19 d = -143.19	903 321 228			
Weibull PH reg	gression			Nu	nber of obs Uncensore Left-censore Right-censore Interval-cens	ed = 5 ed = 38
Log likelihood	d = -143.19228	3			chi2(1) ob > chi2	= 10.93 = 0.0009
	Haz. ratio	Std. err.	Z	P> z	[95% conf.	interval]
treat Radio+Chemo cons	2.498526 .0018503	.7069467 .0013452	3.24 -8.66	0.001	1.434961 .000445	4.350383 .007693
/ln_p	.4785787	.1198973	3.99	0.000	.2435843	.713573
р 1/р	1.613779 .6196635	.1934877 .074296			1.275814 .4898907	2.041272 .7838134

Note: _cons estimates baseline hazard.

The header above the coefficient table summarizes censored and uncensored observations. There are 38 patients who did not experience breast retraction by the last visit, resulting in right-censored observations. There are 5 patients who had breast retraction before their first follow-up, resulting in left-censored observations. There are no uncensored observations, so the remaining 51 observations are interval-censored.

By default, the hazard ratios are reported instead of the natural coefficients. The estimated hazard ratio of the radiotherapy plus chemotherapy is approximately 2.5 with a 95% confidence interval of [1.435, 4.350], indicating significantly higher risk to develop breast retraction using this treatment than radiotherapy only. In other words, the adjuvant chemotherapy increases the risk of breast retraction. The shape parameter is estimated as $\ln(p)$, but p and $1/p = \sigma$ are also reported. The estimated p is greater than 1, indicating that the hazard of breast retraction increases with time.

By default, stintreg uses the PH parameterization for the Weibull model, but we can specify the time option to request the AFT parameterization.

. stintreg i.t	treat, interva	l(ltime rti	me) disti	ribution((weibull) time	e
(iteration log or	mitted)					
Weibull AFT re	egression			Nun	nber of obs	= 94
	0				Uncensore	ed = 0
					Left-censore	ed = 5
					Right-censore	ed = 38
					Interval-cens	s. = 51
				LR	chi2(1)	= 10.93
Log likelihood	d = −143.19228			Pro	ob > chi2	= 0.0009
	L					
	Coefficient	Std. err.	z	P> z	[95% conf.	. interval]
treat						
Radio+Chemo	5674261	.175814	-3.23	0.001	9120151	2228371
_cons	3.899163	.1405986	27.73	0.000	3.623595	4.174731
/ln_p	.4785789	.119897	3.99	0.000	.2435851	.7135726
р	1.613779	.1934873			1.275815	2.041271
1/p	.6196634	.0742958			.4898909	.7838128

With the AFT parameterization, coefficients are reported by default, but we can use the tratio option to display time ratios.

Example 2: Comparing distributions

To compare different models, let's fit the model from example 1 but use the generalized gamma distribution instead. The hazard function of the generalized gamma distribution is extremely flexible, allowing for many different shapes. Weibull, exponential, and lognormal distributions are all special cases of the generalized gamma distribution. Therefore, we can use the generalized gamma model to evaluate and select an appropriate parametric model for the data. When $\kappa = 0$, the generalized gamma model reduces to the lognormal model. When $\kappa = 1$, the generalized gamma model reduces to the Weibull model.

4

. stintreg i.t	creat, interva	l(ltime rti	me) disti	ribution	(ggamma)	
(iteration log or	nitted)					
Generalized ga	amma AFT regre	ssion		Nur	nber of obs	= 94
					Uncensore	ed = 0
					Left-censore	ed = 5
					Right-censore	ed = 38
					Interval-cens	s. = 51
				LR	chi2(1)	= 11.26
Log likelihood	d = -142.71767			Pro	ob > chi2	= 0.0008
						·······
	Coefficient	Std. err.	z	P> z	[95% conf.	interval]
treat						
Radio+Chemo	5696387	.1686355	-3.38	0.001	9001581	2391192
_cons	4.009316	.1721275	23.29	0.000	3.671952	4.346679
/lnsigma	7016456	.2793936	-2.51	0.012	-1.249247	1540442
/kappa	1.532208	.6176603	2.48	0.013	.3216163	2.7428
sigma	.4957688	.1385146			.2867206	.8572341

The Wald test of H_0 : $\kappa = 0$ is reported in the output above. The *p*-value is 0.013, indicating that the lognormal model is not appropriate. We can test the hypothesis that $\kappa = 1$ using the test command:

The above Wald test of H_0 : $\kappa = 1$ has a *p*-value of 0.39, suggesting that the Weibull model may be appropriate for these data.

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Case I interval-censored data

Case I interval-censored data arise when the only survival information available is whether the event of interest occurred before or after the observed time, leading to data in which an observation is either left-censored or right-censored. As such, case I interval-censored data can be viewed as a special case of case II interval-censored data without uncensored and interval-censored on (a, b] observations. Case I interval-censored data occur when subjects are observed only once, and thus we can only know whether the event had already happened before we observed them. Such data are common in demographical studies, where they are also known as current status data. In addition to demographical studies, case I interval-censored data occur in other fields including epidemiological studies, cross-sectional studies, and tumorigenicity experiments. See Huang and Wellner (1997) and Sun (2006) for more information.

The stintreg command requires that case I interval-censored data are recorded by two interval time variables that identify which observations are left-censored and which observations are right-censored.

Example 3: Case I interval-censoring

We consider the data from Hoel and Walburg (1972) on nonlethal lung tumors for 144 male mice. The death time of each mouse (death) and an indicator of whether the lung tumor was present by the time of death (status) were reported. The type of environment (group) in which those mice lived, either

conventional environment (CE) or germ-free environment (GE), was also reported. The goal of this study was to test whether different types of environment had influence on the time of tumor onset for those mice. The lung tumor was known to be nonlethal for the mice. Therefore, the tumor onset time could not be directly observed. The only available information was the observed death time and whether or not the tumor was detected at the time of death.

. use https://www.stata-press.com/data/r19/lungtumor (Lung tumor data for mice)

. table group status

		Tumor status With tumor	Total
Environment			
CE	69	27	96
GE	13	35	48
Total	82	62	144

. list in 26/30

	group	status	death
26.	CE	With tumor	811
27.	CE	With tumor	839
28.	CE	No tumor	45
29.	CE	No tumor	198
30.	CE	No tumor	215

Case I interval-censored data are often stored as shown above: each subject has one variable that represents the observation time and one variable that represents the status of the event of interest. To use stintreg, we must create two time variables to contain the lower and upper endpoints of the intervals. Because case I interval-censored data are either left-censored or right-censored, we first create two new variables, ltime and rtime, that are both equal to the observation time, death, then replace the lower endpoint, ltime, with a missing value if the tumor was detected (status = 1) and replace the upper endpoint, rtime, with a missing value if the tumor was not detected (status = 0).

```
. generate ltime = death
. generate rtime = death
. replace ltime = . if status == 1
(62 real changes made, 62 to missing)
. replace rtime = . if status == 0
(82 real changes made, 82 to missing)
. list in 26/30
```

	group	status	death	ltime	rtime
26.	CE	With tumor	811		811
27.	CE	With tumor	839		839
28.	CE	No tumor	45	45	
29.	CE	No tumor	198	198	
30.	CE	No tumor	215	215	

Now, we fit the model using the exponential distribution.

. stintreg i.g (iteration log of	5 1	al(ltime rti	me) dist	ribution(exponential)		
Exponential PI	H regression			Num	ber of obs	= 1	44
-	-				Uncensore	d =	0
					Left-censore	d =	62
					Right-censore	d =	82
					Interval-cens	. =	0
				LR	chi2(1)	= 16.	09
Log likelihood	d = −81.325875	5		Pro	b > chi2	= 0.00	01
	Haz. ratio	Std. err.	z	P> z	[95% conf.	interva	1]
group							
GE	2.90202	.7728318	4.00	0.000	1.721942	4.8908	28
_cons	.0005664	.0001096	-38.63	0.000	.0003876	.00082	77

Note: _cons estimates baseline hazard.

The estimated hazard for the mice in the germ-free environment is approximately three times the hazard for those in the conventional environment. In other words, the mice in the germ-free environment had higher lung tumor incidence than those in the conventional environment.

```
4
```

Parameterization of ancillary parameters

stintreg's ancillary() and anc2() options allow us to parameterize ancillary parameters in terms of covariates. By default, all ancillary parameters are estimated as being constant. By specifying, for example,

. stintreg x1 x2, interval(ltime rtime) distribution(weibull) ancillary(z1 z2)

the logarithm of the ancillary parameter p is modeled using the linear predictor of z1 and z2. The anc2() option models the second ancillary parameter κ for the generalized log-gamma distribution.

Example 4: Modeling the ancillary parameters

Consider the data described in table 2.3 of Sun (2006) (originally from Richman, Grimes, and Lagakos 1990) on times to resistance to the drug zidovudine for AIDS patients. Covariates of interest are the stage of the disease, stage (0 = early stage, 1 = late stage) and the dose level of the treatment, dose (0 = low dose, 1 = high dose). The time intervals, in months, are stored in variables ltime and rtime.

To investigate whether stage has any effect on time to drug resistance, we fit the Weibull model using stintreg. To later compare results with another model that reports coefficients, we use the nohr option here to display the untransformed coefficients.

. use https://www.stata-pr (Time to zidovudine resist		/r19/aids	s, clear			
. stintreg i.stage, interv	al(ltime rti	me) dist	ribution	(weibull) nohr	•	
(iteration log omitted)						
Weibull PH regression			Nur	mber of obs	= 3	1
-				Uncensore	ed =	0
				Left-censore	ed = 1	5
				Right-censore	ed = 1	3
				Interval-cens	. =	3
			LR	chi2(1)	= 10.0	2
Log likelihood = -13.27946			Pro	ob > chi2	= 0.001	6
Coefficient	Std. err.	Z	P> z	[95% conf.	interval]
1.stage 1.910652	.6604416	2.89	0.004	.6162103	3.20509	4
_cons -7.952868	3.000563	-2.65	0.008	-13.83386	-2.07187	2
/ln_p 1.036662	.397829	2.61	0.009	.2569319	1.81639	3
p 2.81979	1.121794			1.292957	6.14963	5
	.1410846			.1626113	.773420	9

Out of the 31 patients, 13 patients are right-censored, 15 patients are left-censored, and only 3 patients are interval-censored. The estimated coefficient for patients in their late stage of the disease is 1.91; their hazard of resisting zidovudine is approximately exp(1.91) = 6.75 times the hazard for patients in their early stage.

Suppose we believe that the hazards for different dose levels have different shape parameters. We can accommodate this by specifying the ancillary() option.

```
. stintreg i.stage, interval(ltime rtime) distribution(weibull) ancillary(i.dose) note: option nohr is implied if option strata() or ancillary() is specified. (iteration log omitted)
```

(
Weibull PH regression				Nu	mber of obs	=	31
	-				Uncensore	ed =	0
					Left-censore	ed =	15
					Right-censore	ed =	13
					Interval-cens	s. =	3
				LR	chi2(1)	=	12.20
Log likelihoo	d = -11.214877			Pr	ob > chi2	= (0.0005
	Coefficient	Std. err.	Z	P> z	[95% conf	. inte	erval]
ltime							
1.stage	2.795073	1.1675	2.39	0.017	.5068147	5.0	083331
_cons	-10.8462	4.233062	-2.56	0.010	-19.14285	-2.5	549553
ln_p							
1.dose	.1655302	.0874501	1.89	0.058	0058689	.33	369292
_cons	1.252361	.4143254	3.02	0.003	.4402978	2.0	064424

With the ancillary() option, results are displayed as coefficients by default; see the technical note below. From the above results, $\widehat{\ln(p)}_{\text{low}} = 1.25$ for patients with low dose and $\widehat{\ln(p)}_{\text{high}} = 1.25 + 0.17 = 1.42$ for patients with high dose. Thus, $\hat{p}_{\text{low}} = 3.49$ and $\hat{p}_{\text{high}} = 4.14$. When we combine this with the main equation in the model, the estimated hazards are

$$\hat{h}(t_j | \mathbf{x}_j) = \begin{cases} 3.49 \times t_j^{3.49-1} \times \exp\left(-10.85 + 2.80 \times \text{stage}_j\right) & \text{if dose} = 0\\ 4.14 \times t_j^{4.14-1} \times \exp\left(-10.85 + 2.80 \times \text{stage}_j\right) & \text{if dose} = 1 \end{cases}$$

Technical note

When fitting PH models, stintreg, by default, displays hazard ratios. If the strata() option or the ancillary() option (as in our previous example) is specified, stintreg reports coefficients instead. If either of these options is specified, ancillary parameters are no longer constant and are modeled as a function of covariates specified in those options. If any of the covariates from the main equation are used to model ancillary parameters, hazard ratios lose their interpretation. As a precaution, stintreg always displays results as coefficients when those options are used. If we want to compare results with PH models with constant ancillary parameters, we can use the nohr option to display coefficients.

The above argument also applies to time ratios when fitting AFT models. For this reason, the tratio option is not allowed with AFT models whenever strata(), ancillary(), or anc2() is specified.

Stratified estimation

We can fit a stratified model by specifying the strata(*varname*) option. A stratified model means that the coefficients on the covariates are the same across strata, but the intercept and ancillary parameters are allowed to vary for each level of the strata variable.

Example 5: Fitting a stratified model

Continuing with example 4, suppose that we believe that dose affects both the scale and shape of the hazard, and the effect of stage is the same for each level of dose. We refit the Weibull model, but now we also stratify on dose:

. stintreg i.stage, interval(ltime rtime) distribution(weibull) strata(dose) note: option nohr is implied if option strata() or ancillary() is specified. (iteration log omitted) Weibull PH regression Number of obs = 31 Uncensored = 0 Left-censored = 15 Right-censored = 13 Interval-cens. = 3 LR chi2(2) = 12.40 Prob > chi2 = 0.0020 Log likelihood = -11.115197Coefficient Std. err. P>|z| [95% conf. interval] z ltime 2.711532 1.084146 2.50 0.012 .5866441 4.83642 1.stage -2.661873 -0.45 0.651 8.870506 1.dose 5.883975 -14.19425_cons -9.143 4.930796 -1.85 0.064 -18.80718 .5211833 ln_p 1.dose .4538942 .6700991 0.68 0.498 -.85947591.767264 _cons 1.051935 .6190549 1.70 0.089 -.1613906 2.26526

The indicator for level 1 of dose is added to the main equation and to the ancillary equation; level 0 is the baseline and is modeled by the constant terms.

Note that the specification above is the same as fitting the following model:

```
stintreg i.stage i.dose, interval(ltime rtime) distribution(weibull) ///
ancillary(i.dose)
```

By using ancillary() or strata(), we may fit a wide variety of models; see *Stratified estimation* in [ST] **streg** for details. These models may be compared using Wald or likelihood-ratio tests when the models in question are nested or by using the AIC for nonnested models. Modeling of ancillary parameters and stratification is also available for AFT models.

Stored results

```
stintreg stores the following in e():
```

Scalars

e(N)	number of observations
e(N_unc)	number of uncensored observations
e(N_lc)	number of left-censored observations
e(N_rc)	number of right-censored observations
e(N_int)	number of interval-censored observations
e(k)	number of parameters
e(k_eq)	number of equations in e(b)
e(k_eq_model)	number of equations in overall model test
e(k_aux)	number of auxiliary parameters
e(k_dv)	number of dependent variables
e(df_m)	model degrees of freedom
e(11)	log likelihood
e(11_0)	log likelihood, constant-only model
e(N_clust)	number of clusters
e(chi2)	χ^2
e(aux_p)	ancillary parameter (weibull)
-	••• • • •

e(gamma)	ancillary parameter (gompertz, loglogistic)			
e(sigma)	ancillary parameter (ggamma, lnormal)			
e(kappa)	ancillary parameter (ggamma)			
e(epsilon)	tolerance for uncensored observations			
e(p)	<i>p</i> -value for model test			
e(rank)	rank of e(V)			
e(rank0)	rank of e(V), constant-only model			
e(ic)	number of iterations			
e(rc)	return code			
e(converged)	1 if converged, 0 otherwise			
Macros				
e(cmd)	model or regression name			
e(cmd2)	stintreg			
e(cmdline)	command as typed			
e(depvar)	names of time interval variables specified in interval()			
e(distribution)	distribution			
e(strata)	stratum variable			
e(title)	title in estimation output			
e(clustvar)	name of cluster variable			
e(wtype)	weight type			
e(wexp)	weight expression			
e(vce)	vcetype specified in vce()			
e(vcetype)	title used to label Std. err.			
e(frm2)	hazard or time			
e(chi2type)	Wald or LR; type of model χ^2 test			
e(offset1)	offset for main equation			
e(opt)	type of optimization			
e(which)	max or min; whether optimizer is to perform maximization or minimization			
e(ml_method)	type of ml method			
e(user)	name of likelihood-evaluator program			
e(technique)	maximization technique			
e(properties)	b V			
e(estat_cmd)	program used to implement estat			
e(predict)	program used to implement predict			
e(predict_sub)	predict subprogram			
e(marginsok)	predictions allowed by margins			
e(marginsnotok)	predictions disallowed by margins			
e(asbalanced)	factor variables fvset as asbalanced			
e(asobserved)	factor variables fvset as asobserved			
Matrices				
e(b)	coefficient vector			
e(Cns)	constraints matrix			
e(ilog)	iteration log (up to 20 iterations)			
e(gradient)	gradient vector			
e(V)	variance–covariance matrix of the estimators			
e(V_modelbased)	model-based variance			
Functions				
e(sample)	marks estimation sample			
c (bampro)	marks commuton sumple			

In addition to the above, the following is stored in r():

Matrices

r(table) matrix containing the coefficients with their standard errors, test statistics, *p*-values, and confidence intervals

Note that results stored in r() are updated when the command is replayed and will be replaced when any r-class command is run after the estimation command.

Methods and formulas

Methods and formulas are presented under the following headings:

Introduction Distributions and parameterizations Parameter estimation using interval-censored data

Introduction

Consider event-time data that consists of n independent observations. Let t_j represent the survival time for the event of interest for observation j, j = 1, ..., n.

For a given survivor function, S(t), the density function is obtained as

$$f(t) = -\frac{d}{dt}S(t)$$

and the hazard function (the instantaneous rate of failure) is obtained as

$$h(t) = \frac{f(t)}{S(t)} = -\frac{\log S(t)}{dt}$$

Let \mathbf{x}_j denote a vector of covariates for observation j, and let β denote a vector of regression coefficients. Let $S_j(t) = S(t|\mathbf{x} = \mathbf{x}_j)$ be the covariate-adjusted survivor function and similarly define $h_j(t)$ and $f_j(t)$.

stintreg supports six survival distributions: exponential, Weibull, Gompertz, lognormal, loglogistic, and generalized gamma; and two parameterizations for the effects of covariates: PH and AFT. The parameterization and ancillary parameters for each distribution are summarized in table 1 below.

Distributions and parameterizations

The PH model assumes that the hazard function has the form

$$h_j(t) = h_0(t) \exp\left(\mathbf{x}_j \boldsymbol{\beta}\right)$$

for some baseline hazard function $h_0(t)$. For the stintreg command, $h_0(t)$ is assumed to be parametric and the supported distributions are exponential, Weibull, and Gompertz. This model specifies that the covariates have a multiplicative effect on the hazard function. The covariate-adjusted survivor function $S_i(t)$ is obtained as

$$S_i(t) = \{S_0(t)\} \exp(\mathbf{x}_j \beta)$$

where the baseline survivor function $S_0(t) = \exp\{-\int_0^t h_0(s)ds\}$.

In the AFT model, the natural logarithm of the survival time, $\log t$, is expressed as a linear function of the covariates, yielding the linear model

$$\log t_j = \mathbf{x}_j \boldsymbol{\beta} + z_j$$

where z_j is the error term with density f(). The distributional form of the error term determines the regression model. If we let f() be the normal density, the lognormal regression model for t_j is obtained. Similarly, by letting f() be the logistic density, the loglogistic regression is obtained. Setting f() equal to the extreme-value density yields the exponential and the Weibull regression models. The effect of covariates is also multiplicative, but on time t_j , by a factor of $\exp(-\mathbf{x}_j\beta)$. Depending on whether this factor is greater or less than one, time is either accelerated or decelerated.

Table 1 below describes the supported survival models, their parameterizations, and the corresponding ancillary parameters.

Distribution	Metric	Survivor function	Parameterization	Ancillary parameters
Exponential	PH	$\exp(-\lambda_j t_j)$	$\lambda_j = \exp(\mathbf{x}_j \boldsymbol{\beta})$	
Exponential	AFT	$\exp(-\lambda_j t_j)$	$\lambda_j = \exp(-\mathbf{x}_j \boldsymbol{\beta})$	
Weibull	PH	$\exp(-\lambda_j t_j^p)$	$\lambda_j = \exp(\mathbf{x}_j \boldsymbol{\beta})$	p
Weibull	AFT	$\exp(-\lambda_j t_j^p)$	$\lambda_j = \exp(-p \mathbf{x}_j \boldsymbol{\beta})$	p
Gompertz	PH	$\exp\{-\lambda_j\gamma^{-1}(e^{\gamma t_j}-1)\}$	$\lambda_j = \exp(\mathbf{x}_j \boldsymbol{\beta})$	γ
Lognormal	AFT	$1 - \Phi\left\{\frac{\log{(t_j)} - \mu_j}{\sigma}\right\}$	$\mu_j = \mathbf{x}_j \boldsymbol{\beta}$	σ
Loglogistic	AFT	$\{1+(\lambda_{j}t_{j})^{1/\gamma}\}^{-1}$	$\lambda_j = \exp(-\mathbf{x}_j \boldsymbol{\beta})$	γ
Generalized gamma				
$ \text{if} \ \kappa > 0 \\$	AFT	$1-I(\gamma,u)$	$\mu_j = \mathbf{x}_j \boldsymbol{\beta}$	σ, κ
if $\kappa = 0$	AFT	$1 - \Phi(z)$	$\mu_j = \mathbf{x}_j \boldsymbol{\beta}$	σ,κ
$\inf \kappa < 0$	AFT	$I(\gamma, u)$	$\mu_j = \mathbf{x}_j \boldsymbol{\beta}$	σ, κ

Table 1. Parametric	survival	distributions	supported by	stintreg

where $\Phi(z)$ is the standard normal cumulative distribution. For the generalized gamma, $\gamma = |\kappa|^{-2}$, $u = \gamma \exp(|\kappa|z)$, I(a, x) is the incomplete gamma function, and $z = \operatorname{sign}(\kappa) \{ \log(t_i) - \mu_i \} / \sigma$.

Parameter estimation using interval-censored data

Suppose that t_j is not observed and that only the lower and upper endpoints of the time interval, t_{lj} and t_{uj} , where $t_j \in (t_{lj}, t_{uj}]$, are observed. stintreg estimates β and the ancillary parameters via maximum likelihood. For interval-censored observations, the log likelihood is given by

$$\log L = \sum_{j=1}^n \ \log \left\{ S_j(t_{lj}) - S_j(t_{uj}) \right\}$$

Implicit in the above log-likelihood expression are the regression parameters, β , and the ancillary parameters, because both are components of the chosen $S_j(t)$; see table 1.

For case II interval-censored data, the log likelihood can be written as

$$\begin{split} \log L = & \sum_{j \in UC} \log f_j(t_{lj}) + \sum_{j \in RC} \log S_j(t_{lj}) + \sum_{j \in LC} \log \left\{ 1 - S_j(t_{uj}) \right\} \\ & + \sum_{j \in IC} \log \left\{ S_j(t_{lj}) - S_j(t_{uj}) \right\} \end{split}$$

where the set UC contains uncensored observations, RC contains right-censored observations, LC contains left-censored observations, and IC contains interval-censored observations.

For case I interval-censored data, with only right-censored and left-censored observations, the log likelihood reduces to

$$\log L = \sum_{j \in RC} \log S_j(t_{lj}) + \sum_{j \in LC} \log \left\{1 - S_j(t_{uj})\right\}$$

Specifying ancillary(), anc2(), or strata() will parameterize the ancillary parameter(s) by using the linear predictor, $\mathbf{z}_j \alpha_z$, where the covariates, \mathbf{z}_j , need not be distinct from \mathbf{x}_j . Here stintreg will report estimates of α_z in addition to estimates of β . The log likelihood here is simply the log likelihood given above, with $\mathbf{z}_j \alpha_z$ substituted for the ancillary parameter. If the ancillary parameter is constrained to be strictly positive, its logarithm is parameterized instead; that is, we substitute the linear predictor for the logarithm of the ancillary parameter in the above log likelihood. The gamma model has two ancillary parameters, σ and κ ; we parameterize σ by using ancillary() and κ by using anc2(), and the linear predictors used for each may be distinct. Specifying strata() includes indicator variables for the strata in the main equation, and uses them to parameterize any ancillary parameters that exist for the chosen model.

This command supports the Huber/White/sandwich estimator of the variance and its clustered version using vce(robust) and vce(cluster *clustvar*), respectively. See [P] **_robust**, particularly *Maximum likelihood estimators* and *Methods and formulas*. If the assumption of independence of the observations is highly questionable, this means that the conventional estimate of variance is not appropriate. We strongly advise that you use the vce(robust) and vce(cluster *clustvar*) options here.

stintreg also supports estimation with survey data. For details on VCEs with survey data, see [SVY] Variance estimation.

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Also see

- [ST] stintreg postestimation Postestimation tools for stintreg
- [ST] stcurve Plot the survivor or related function after streg, stcox, and more
- [ST] stcox Cox proportional hazards model
- [ST] stintcox Cox proportional hazards model for interval-censored survival-time data
- [ST] streg Parametric survival models
- [SVY] svy estimation Estimation commands for survey data
- [U] 20 Estimation and postestimation commands

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