Title

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| streg — Parametric survival | models | | |
|---|--|--|-----------------------|
| Syntax Remarks and examples Also see | Menu Stored results | Description Methods and formulas | Options References |
| Syntax | | | |
| streg $[varlist]$ $[if]$ $[in]$ | [, options] | | |
| options | Description | | |
| Model <u>nocon</u> stant <u>d</u> istribution(<u>e</u> xponential) <u>d</u> istribution(<u>log</u> logistic) <u>d</u> istribution(<u>llog</u> istic) <u>d</u> istribution(<u>w</u> eibull) <u>d</u> istribution(<u>log</u> normal) <u>d</u> istribution(<u>lnormal</u>) <u>d</u> istribution(<u>gamma</u>) <u>frailty(gamma</u>) <u>frailty(i</u> nvgaussian) <u>time</u> Model 2 | Gompertz sur loglogistic sur synonym for Weibull survi lognormal sur synonym for generalized g gamma frailty inverse-Gauss | urvival distribution vival distribution rvival distribution distribution(loglogis val distribution rvival distribution distribution(lognorma amma survival distribution | |
| <pre>Model 2 strata(varname) offset(varname) shared(varname) ancillary(varlist) anc2(varlist) constraints(constraints) collinear</pre> | shared frailty use <i>varlist</i> to use <i>varlist</i> to | <i>me</i> in model with coefficient ID variable model the first ancillary p model the second ancillary d linear constraints | arameter |
| SE/Robust vce(<i>vcetype</i>) | | be oim, <u>r</u> obust, <u>cl</u> uster , or <u>jack</u> knife | clustvar, opg, |

| Reporting | |
|---------------------|---|
| <u>l</u> evel(#) | set confidence level; default is level(95) |
| nohr | do not report hazard ratios |
| tr | report time ratios |
| <u>nos</u> how | do not show st setting information |
| <u>nohead</u> er | suppress header from coefficient table |
| <u>nolr</u> test | do not perform likelihood-ratio test |
| <u>nocnsr</u> eport | do not display constraints |
| display_options | control 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>coefl</u> egend | display legend instead of statistics |

You must stset your data before using streg; see [ST] stset.

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

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

vce(bootstrap) and vce(jackknife) are not allowed with the mi estimate prefix; see [MI] mi estimate.

shared(), vce(), and noheader are not allowed with the svy prefix; see [SVY] svy.

fweights, iweights, and pweights may be specified using stset; see [ST] stset. However, weights may not be specified if you are using the bootstrap prefix with the streg command.

coeflegend does not appear in the dialog box.

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

Menu

Statistics > Survival analysis > Regression models > Parametric survival models

Description

streg performs maximum likelihood estimation for parametric regression survival-time models. streg can be used with single- or multiple-record or single- or multiple-failure st data. Survival models currently supported are exponential, Weibull, Gompertz, lognormal, loglogistic, and generalized gamma. Parametric frailty models and shared-frailty models are also fit using streg.

Also see [ST] stcox for proportional hazards models.

Options

_ Model]

noconstant; see [R] estimation options.

distribution(*distname*) specifies the survival model to be fit. A specified distribution() is remembered from one estimation to the next when distribution() is not specified.

For instance, typing streg x1 x2, distribution(weibull) fits a Weibull model. Subsequently, you do not need to specify distribution(weibull) to fit other Weibull regression models.

All Stata estimation commands, including streg, redisplay results when you type the command name without arguments. To fit a model with no explanatory variables, type streg, distribution(*distname*)....

frailty(gamma | invgaussian) specifies the assumed distribution of the frailty, or heterogeneity. The estimation results, in addition to the standard parameter estimates, will contain an estimate of the variance of the frailties and a likelihood-ratio test of the null hypothesis that this variance is zero. When this null hypothesis is true, the model reduces to the model with frailty(distname) not specified.

A specified frailty() is remembered from one estimation to the next when distribution() is not specified. When you specify distribution(), the previously remembered specification of frailty() is forgotten.

time specifies that the model be fit in the accelerated failure-time metric rather than in the log relative-hazard 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.

time must be specified at estimation.

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 unique to each stratum) are then obtained. This option is not available if frailty(distname) is specified.

offset(varname); see [R] estimation options.

shared(varname) is valid with frailty() and specifies a variable defining those groups over which the frailty is shared, analogous to a random-effects model for panel data where varname defines the panels. frailty() specified without shared() treats the frailties as occurring at the observation level.

A specified shared() is remembered from one estimation to the next when distribution() is not specified. When you specify distribution(), the previously remembered specification of shared() is forgotten.

shared() may not be used with distribution(gamma), vce(robust), vce(cluster clustvar), vce(opg), the svy prefix, or in the presence of delayed entries or gaps.

If shared() is specified without frailty() and there is no remembered frailty() from the previous estimation, frailty(gamma) is assumed to provide behavior analogous to stcox; see [ST] stcox.

ancillary(*varlist*) specifies that the ancillary parameter for the Weibull, lognormal, Gompertz, and loglogistic distributions and that the first ancillary parameter (sigma) of the generalized log-gamma distribution be estimated as a linear combination of *varlist*. This option may not be used with frailty(*distname*).

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 (kappa) for the generalized log-gamma distribution be estimated as a linear combination of *varlist*. This option may not be used with frailty(*distname*).

constraints(constraints), collinear; see [R] estimation options.

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).

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

tr may be specified at estimation or upon replay.

noshow prevents streg from showing the key st variables. This option is rarely used because most people type stset, show or stset, noshow to set once and for all whether they want to see these variables mentioned at the top of the output of every st command; see [ST] stset.

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

- nolrtest is valid only with frailty models, in which case it suppresses the likelihood-ratio test for significant frailty.
- nocnsreport; see [R] estimation options.
- display_options: 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 option is available with streg but is not shown in the dialog box: coeflegend; see [R] estimation options.

Remarks and examples

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Remarks are presented under the following headings:

Introduction Distributions Weibull and exponential models Gompertz model Lognormal and loglogistic models Generalized gamma model Examples Parameterization of ancillary parameters Stratified estimation (Unshared-) frailty models Shared-frailty models

Introduction

What follows is a brief summary of what you can do with streg. For a complete tutorial, see Cleves et al. (2010), which devotes four chapters to this topic.

Two often-used models for adjusting survivor functions for the effects of covariates are the accelerated failure-time (AFT) model and the multiplicative or proportional hazards (PH) model. 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 \mathbf{x}_j is a vector of covariates, $\boldsymbol{\beta}$ is a vector of regression coefficients, and z_j is the error 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 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 the AFT model is to change the time scale by a factor of $\exp(-\mathbf{x}_j\beta)$. Depending on whether this factor is greater or less than 1, time is either accelerated or decelerated (degraded). That is, if a subject at baseline experiences a probability of survival past time t equal to S(t), then a subject with covariates \mathbf{x}_j would have probability of survival past time t equal to S() evaluated at the point $\exp(-\mathbf{x}_j\beta)t$, instead. Thus accelerated failure time does not imply a positive acceleration of time with the increase of a covariate but instead implies a deceleration of time or, equivalently, an increase in the expected waiting time for failure.

In the PH model, the concomitant covariates have a multiplicative effect on the hazard function

$$h(t_j) = h_0(t)g(\mathbf{x}_j)$$

for some $h_0(t)$, and for $g(\mathbf{x}_j)$, a nonnegative function of the covariates. A popular choice, and the one adopted here, is to let $g(\mathbf{x}_j) = \exp(\mathbf{x}_j\beta)$. The function $h_0(t)$ may either be left unspecified, yielding the Cox proportional hazards model (see [ST] stcox), or take a specific parametric form. For the streg command, $h_0(t)$ is assumed to be parametric. Three regression models are currently implemented as PH models: the exponential, Weibull, and Gompertz 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.

The above model allows for the presence of an intercept term, β_0 , within $\mathbf{x}_j\beta$. Thus what is commonly referred to as the baseline hazard function—the hazard when all covariates are zero—is actually equal to $h_0(t) \exp(\beta_0)$. That is, the intercept term serves to scale the baseline hazard. Of course, specifying noconstant suppresses the intercept or equivalently constrains β_0 to equal zero.

streg is suitable only for data that have been stset. By stsetting your data, you define the variables _t0, _t, and _d, which serve as the trivariate response variable (t_0, t, d) . Each response corresponds to a period under observation, $(t_0, t]$, resulting in either failure (d = 1) or right-censoring (d = 0) at time t. As a result, streg is appropriate for data exhibiting delayed entry, gaps, time-varying covariates, and even multiple-failure data.

Distributions

Six parametric survival distributions are currently supported by streg. The parameterization and ancillary parameters for each distribution are summarized in table 1:

| 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 | | | | |
| 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 |
| if $\kappa < 0$ | AFT | $I(\gamma, u)$ | $\mu_j = \mathbf{x}_j \boldsymbol{\beta}$ | σ, κ |

Table 1. Parametric survival distributions supported by streg

where PH = proportional hazards, AFT = accelerated failure time, and $\Phi(z)$ 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 $z = \operatorname{sign}(\kappa) \{ \log(t_j) - \mu_j \} / \sigma$.

Plotted in figure 1 are example hazard functions for five of the six distributions. The exponential hazard (not separately plotted) is a special case of the Weibull hazard when the Weibull ancillary parameter p = 1. The generalized gamma (not plotted) is extremely flexible and therefore can take many shapes.



Figure 1. Example plots of hazard functions

Weibull and exponential models

The Weibull and exponential models are parameterized as both PH and AFT models. The Weibull distribution is suitable for modeling data with monotone hazard rates that either increase or decrease exponentially with time, whereas the exponential distribution is suitable for modeling data with constant hazard (see figure 1).

For the PH model, $h_0(t) = 1$ for exponential regression, and $h_0(t) = p t^{p-1}$ for Weibull regression, where p is the shape parameter to be estimated from the data. Some authors refer not to p but to $\sigma = 1/p$.

The AFT model is written as

$$\log(t_j) = \mathbf{x}_j \boldsymbol{\beta}^* + z_j$$

where z_j has an extreme-value distribution scaled by σ . Let β be the vector of regression coefficients derived from the PH model so that $\beta^* = -\sigma\beta$. This relationship holds only if the ancillary parameter, p, is a constant; it does not hold when the ancillary parameter is parameterized in terms of covariates.

streg uses, by default, for the exponential and Weibull models, the proportional-hazards metric simply because it eases comparison with those results produced by stcox (see [ST] stcox). You can, however, specify the time option to choose the accelerated failure-time parameterization.

The Weibull hazard and survivor functions are

$$h(t) = p\lambda t^{p-1}$$

$$S(t) = \exp(-\lambda t^p)$$

where λ is parameterized as described in table 1. If p = 1, these functions reduce to those of the exponential.

Gompertz model

The Gompertz regression is parameterized only as a PH model. First described in 1825, this model has been extensively used by medical researchers and biologists modeling mortality data. The Gompertz distribution implemented is the two-parameter function as described in Lee and Wang (2003), with the following hazard and survivor functions:

$$h(t) = \lambda \exp(\gamma t)$$
$$S(t) = \exp\{-\lambda \gamma^{-1} (e^{\gamma t} - 1)\}$$

The model is implemented by parameterizing $\lambda_j = \exp(\mathbf{x}_j \boldsymbol{\beta})$, implying that $h_0(t) = \exp(\gamma t)$, where γ is an ancillary parameter to be estimated from the data.

This distribution is suitable for modeling data with monotone hazard rates that either increase or decrease exponentially with time (see figure 1).

When γ is positive, the hazard function increases with time; when γ is negative, the hazard function decreases with time; and when γ is zero, the hazard function is equal to λ for all t, so the model reduces to an exponential.

Some recent survival analysis texts, such as Klein and Moeschberger (2003), restrict γ to be strictly positive. If $\gamma < 0$, then as t goes to infinity, the survivor function, S(t), exponentially decreases to a nonzero constant, implying that there is a nonzero probability of never failing (living forever). That is, there is always a nonzero hazard rate, yet it decreases exponentially. By restricting γ to be positive, we know that the survivor function always goes to zero as t tends to infinity.

Although the above argument may be desirable from a mathematical perspective, in Stata's implementation, we took the more traditional approach of not restricting γ . We did this because, in survival studies, subjects are not monitored forever—there is a date when the study ends, and in many investigations, specifically in medical research, an exponentially decreasing hazard rate is clinically appealing.

Lognormal and loglogistic models

The lognormal and loglogistic models are implemented only in the AFT form. These two distributions are similar and tend to produce comparable results. For the lognormal distribution, the natural logarithm of time follows a normal distribution; for the loglogistic distribution, the natural logarithm of time follows a logistic distribution.

The lognormal survivor and density functions are

$$S(t) = 1 - \Phi\left\{\frac{\log(t) - \mu}{\sigma}\right\}$$

$$f(t) = \frac{1}{t\sigma\sqrt{2\pi}} \exp\left[\frac{-1}{2\sigma^2} \left\{\log(t) - \mu\right\}^2\right]$$

where $\Phi(z)$ is the standard normal cumulative distribution function.

The lognormal regression is implemented by setting $\mu_j = \mathbf{x}_j \boldsymbol{\beta}$ and treating the standard deviation, σ , as an ancillary parameter to be estimated from the data.

The loglogistic regression is obtained if z_j has a logistic density. The loglogistic survivor and density functions are

$$S(t) = \{1 + (\lambda t)^{1/\gamma}\}^{-1}$$

$$f(t) = \frac{\lambda^{1/\gamma} t^{1/\gamma-1}}{\gamma \left\{1 + (\lambda t)^{1/\gamma}\right\}^2}$$

This model is implemented by parameterizing $\lambda_j = \exp(-\mathbf{x}_j\beta)$ and treating the scale parameter γ as an ancillary parameter to be estimated from the data.

Unlike the exponential, Weibull, and Gompertz distributions, the lognormal and the loglogistic distributions are indicated for data exhibiting nonmonotonic hazard rates, specifically initially increasing and then decreasing rates (figure 1).

Thus far we have considered the exponential, Weibull, lognormal, and loglogistic models. These models are sufficiently flexible for many datasets, but further flexibility can be obtained with the generalized gamma model, described below. Alternatively, you might consider using a Royston–Parmar model (Royston and Parmar 2002; Lambert and Royston 2009). Royston–Parmar models are highly flexible alternatives to the exponential, Weibull, lognormal, and loglogistic models that allow extension from proportional hazards to proportional odds and to scaled probit models. Additional flexibility can be obtained with restricted cubic spline functions as alternatives to the linear functions of log time considered in *Introduction*. See Royston and Lambert (2011) for a thorough treatment of this topic.

Generalized gamma model

The generalized gamma model is implemented only in the AFT form. The three-parameter generalized gamma survivor and density functions are

$$S(t) = \begin{cases} 1 - I(\gamma, u), & \text{if } \kappa > 0\\ 1 - \Phi(z), & \text{if } \kappa = 0\\ I(\gamma, u), & \text{if } \kappa < 0 \end{cases}$$
$$f(t) = \begin{cases} \frac{\gamma^{\gamma}}{\sigma t \sqrt{\gamma} \Gamma(\gamma)} \exp\left(z\sqrt{\gamma} - u\right), & \text{if } \kappa \neq 0\\ \frac{1}{\sigma t \sqrt{2\pi}} \exp(-z^2/2), & \text{if } \kappa = 0 \end{cases}$$

where $\gamma = |\kappa|^{-2}$, $z = \operatorname{sign}(\kappa) \{ \log(t) - \mu \} / \sigma$, $u = \gamma \exp(|\kappa|z)$, $\Phi(z)$ is the standard normal cumulative distribution function, and I(a, x) is the incomplete gamma function. See the gammap(a,x) entry in [D] functions to see how the incomplete gamma function is implemented in Stata.

This model is implemented by parameterizing $\mu_j = \mathbf{x}_j \boldsymbol{\beta}$ and treating the parameters κ and σ as ancillary parameters to be estimated from the data.

The hazard function of the generalized gamma distribution is extremely flexible, allowing for many possible shapes, including as special cases the Weibull distribution when $\kappa = 1$, the exponential when $\kappa = 1$ and $\sigma = 1$, and the lognormal distribution when $\kappa = 0$. The generalized gamma model is, therefore, commonly used for evaluating and selecting an appropriate parametric model for the data. The Wald or likelihood-ratio test can be used to test the hypotheses that $\kappa = 1$ or that $\kappa = 0$.

Examples

Example 1

The Weibull distribution provides a good illustration of streg because this distribution is parameterized as both AFT and PH and serves to compare and contrast the two approaches.

We wish to analyze an experiment testing the ability of emergency generators with new-style bearings to withstand overloads. This dataset is described in [ST] **stcox**. This time, we wish to fit a Weibull model:

```
. use http://www.stata-press.com/data/r13/kva
(Generator experiment)
. streg load bearings, distribution(weibull)
         failure _d: 1 (meaning all fail)
   analysis time _t: failtime
Fitting constant-only model:
Iteration 0:
               log likelihood = -13.666193
               \log likelihood = -9.7427276
Iteration 1:
Iteration 2:
               \log likelihood = -9.4421169
Iteration 3:
               \log likelihood = -9.4408287
               \log likelihood = -9.4408286
Iteration 4:
Fitting full model:
Iteration 0:
               log likelihood = -9.4408286
Iteration 1:
               log likelihood = -2.078323
               log likelihood = 5.2226016
Iteration 2:
               log likelihood = 5.6745808
Iteration 3:
Iteration 4:
               log likelihood = 5.6934031
Iteration 5:
               log likelihood = 5.6934189
Iteration 6:
               log likelihood = 5.6934189
Weibull regression -- log relative-hazard form
No. of subjects =
                             12
                                                     Number of obs
                                                                      =
                                                                               12
No. of failures =
                             12
Time at risk
                            896
                                                     LR chi2(2)
                                                                            30.27
                                                                      =
Log likelihood
                     5.6934189
                                                     Prob > chi2
                                                                           0.0000
               =
                                                                      =
               Haz. Ratio
                             Std. Err.
                                                  P>|z|
                                                            [95% Conf. Interval]
          _t
                                             z
                                                  0.000
        load
                  1.599315
                             .1883807
                                           3.99
                                                            1.269616
                                                                         2.014631
                  .1887995
                                          -2.40
                                                  0.016
                                                            .0483546
                                                                         .7371644
    bearings
                             .1312109
       _cons
                  2.51e-20
                             2.66e-19
                                         -4.26
                                                  0.000
                                                            2.35e-29
                                                                         2.68e-11
                                          8.85
                                                  0.000
                                                            1.597414
                                                                         2.505691
       /ln_p
                 2.051552
                             .2317074
                  7.779969
                             1.802677
                                                            4.940241
                                                                         12.25202
           р
                  .1285352
                             .0297826
                                                             .0816192
                                                                         .2024193
         1/p
```

Because we did not specify otherwise, the estimation took place in the hazard metric, which is the default for distribution(weibull). The estimates are directly comparable to those produced by stcox: stcox estimated a hazard ratio of 1.526 for load and 0.0636 for bearings.

However, we estimated the baseline hazard function as well, assuming that it is Weibull. The estimates are the full maximum-likelihood estimates. The shape parameter is fit as $\ln p$, but streg then reports p and $1/p = \sigma$ so that you can think about the parameter however you wish.

We find that p is greater than 1, which means that the hazard of failure increases with time and, here, increases dramatically. After 100 hours, the bearings are more than 1 million times more likely to fail per second than after 10 hours (or, to be precise, $(100/10)^{7.78-1}$). From our knowledge of generators, we would expect this; it is the accumulation of heat due to friction that causes bearings to expand and seize.

4

Technical note

Regression results are often presented in a metric other than the natural regression coefficients, that is, as hazard ratios, relative risk ratios, odds ratios, etc. In those cases, standard errors are calculated using the delta method.

However, the Z test and p-values given are calculated from the natural regression coefficients and standard errors. Although a test based on, say, a hazard ratio and its standard error would be asymptotically equivalent to that based on a regression coefficient, in real samples a hazard ratio will tend to have a more skewed distribution because it is an exponentiated regression coefficient. Also, it is more natural to think of these tests as testing whether a regression coefficient is nonzero, rather than testing whether a transformed regression coefficient is unequal to some nonzero value (one for a hazard ratio).

Finally, the confidence intervals given are obtained by transforming the endpoints of the corresponding confidence interval for the untransformed regression coefficient. This ensures that, say, strictly positive quantities such as hazard ratios have confidence intervals that do not overlap zero.

Example 2

The previous estimation took place in the PH metric, and exponentiated coefficients—hazard ratios—were reported. If we want to see the unexponentiated coefficients, we could redisplay results and specify the nohr option:

| ssion log : | relative-haz | ard form | | | |
|-------------|-----------------|--|---|--|--|
| ;s = | 12 | | Numb | per of obs | = 12 |
| es = | 12 | | | | |
| = | 896 | | | | |
| | | | LR c | chi2(2) = | = 30.27 |
| 1 = 5.6934 | 4189 | | Prob | o≻chi2 ≕ | = 0.0000 |
| | | | | | |
| Coef. | Std. Err. | z | P> z | [95% Conf | . Interval] |
| .4695753 | .1177884 | 3.99 | 0.000 | .2387143 | .7004363 |
| -1.667069 | .6949745 | -2.40 | 0.016 | -3.029194 | 3049443 |
| -45.13191 | 10.60663 | -4.26 | 0.000 | -65.92053 | -24.34329 |
| 2.051552 | .2317074 | 8.85 | 0.000 | 1.597414 | 2.505691 |
| 7.779969 | 1.802677 | | | 4.940241 | 12.25202 |
| .1285352 | .0297826 | | | .0816192 | .2024193 |
| | <pre>is =</pre> | <pre>iss = 12 iss = 1</pre> | es = 12 = 896 1 = 5.6934189 Coef. Std. Err. z .4695753 .1177884 3.99 -1.667069 .6949745 -2.40 -45.13191 10.60663 -4.26 2.051552 .2317074 8.85 7.779969 1.802677 | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |

Example 3

We could just as well have fit this model in the AFT metric:

| . streg load b | pearings, d(w | eibull) time | e nolog | | | |
|--|------------------------------|----------------------|-----------|-------|----------------------|----------------------|
| | ire _d: 1 (m ime _t: fail | 0 | ail) | | | |
| Weibull regres | ssion acce | lerated fail | lure-time | form | | |
| No. of subject No. of failure Time at risk | es = | 12 12 896 | | Numl | ber of obs | = 12 |
| | | | | LR (| chi2(2) = | = 30.27 |
| Log likelihood | d = 5.693 | 4189 | | Prol | b > chi2 = | = 0.0000 |
| t | Coef. | Std. Err. | z | P> z | [95% Conf | . Interval] |
| load | 060357 | .0062214 | -9.70 | 0.000 | 0725507 | 0481632 |
| bearings | .2142771 | .0746451 | 2.87 | 0.004 | .0679753 | .3605789 |
| _cons | 5.80104 | .1752301 | 33.11 | 0.000 | 5.457595 | 6.144485 |
| /ln_p | 2.051552 | .2317074 | 8.85 | 0.000 | 1.597414 | 2.505691 |
| p 1/p | 7.779969 .1285352 | 1.802677 .0297826 | | | 4.940241 .0816192 | 12.25202 .2024193 |

This is the same model we previously fit, but it is presented in a different metric. Calling the previous coefficients b, these coefficients are $-\sigma b = -b/p$. For instance, in the previous example, the coefficient on load was reported as 0.4695753, and -0.4695753/7.779969 = -0.06035696. d() is a convenient shorthand for distribution().

Example 4

streg may also be applied to more complicated data. Below we have multiple records per subject on a failure that can occur repeatedly:

```
. use http://www.stata-press.com/data/r13/mfail3
```

. stdescribe

| | | | per subj | ject | |
|--------------------|--------|----------|----------|--------|-----|
| Category | total | mean | min | median | max |
| no. of subjects | 926 | | | | |
| no. of records | 1734 | 1.87257 | 1 | 2 | 4 |
| (first) entry time | | 0 | 0 | 0 | 0 |
| (final) exit time | | 470.6857 | 1 | 477 | 960 |
| subjects with gap | 6 | | | | |
| time on gap if gap | 411 | 68.5 | 16 | 57.5 | 133 |
| time at risk | 435444 | 470.2419 | 1 | 477 | 960 |
| failures | 808 | .8725702 | 0 | 1 | 3 |

In this dataset, subjects have up to four records (most have two) and have up to three failures (most have one) and, although you cannot tell from the above output, the data have time-varying covariates, as well. There are even six subjects with gaps in their histories, meaning that, for a while, they went unobserved. Although we could estimate in the AFT metric, it is easier to interpret results in the PH metric (or the log relative-hazard metric, as it is also known):

```
. streg x1 x2, d(weibull) vce(robust)
Fitting constant-only model:
                log pseudolikelihood = -1398.2504
Iteration 0:
Iteration 1:
                log pseudolikelihood = -1382.8224
                log pseudolikelihood = -1382.7457
Iteration 2:
Iteration 3:
               log pseudolikelihood = -1382.7457
Fitting full model:
Iteration 0:
                log pseudolikelihood = -1382.7457
                log pseudolikelihood = -1328.4186
Iteration 1:
Iteration 2:
               log pseudolikelihood = -1326.4483
Iteration 3:
                log pseudolikelihood = -1326.4449
Iteration 4:
                log pseudolikelihood = -1326.4449
Weibull regression -- log relative-hazard form
No. of subjects
                      =
                                  926
                                                      Number of obs
                                                                              1734
                                                                       =
No. of failures
                                  808
                      =
Time at risk
                      =
                              435444
                                                      Wald chi2(2)
                                                                            154.45
Log pseudolikelihood =
                          -1326.4449
                                                     Prob > chi2
                                                                            0.0000
                                                                       =
                                     (Std. Err. adjusted for 926 clusters in id)
                              Robust
          _t
               Haz. Ratio
                             Std. Err.
                                             z
                                                  P>|z|
                                                             [95% Conf. Interval]
                  2.240069
                             .1812848
                                           9.97
                                                  0.000
                                                             1.911504
                                                                          2.625111
          x1
                  .3206515
                             .0504626
                                          -7.23
                                                  0.000
                                                             .2355458
                                                                           .436507
          x2
                                                  0.000
                  .0006962
                             .0001792
                                         -28.25
                                                             .0004204
                                                                           .001153
       cons
                  .1771265
                             .0310111
                                           5.71
                                                   0.000
                                                             .1163458
                                                                          .2379071
       /ln_p
                  1.193782
                              .0370205
                                                                          1.268591
           р
                                                             1.123384
                  .8376738
                             .0259772
                                                                          .8901674
         1/p
                                                             .7882759
```

A one-unit change in x1 approximately doubles the hazard of failure, whereas a one-unit change in x2 cuts the hazard to one-third its previous value. We also see that these data are close to being exponentially distributed; p is nearly 1.

Above we mentioned that interpreting results in the PH metric is easier, though regression coefficients are not difficult to interpret in the AFT metric. A positive coefficient means that time is decelerated by a unit increase in the covariate in question. This may seem awkward, but think of this instead as a unit increase in the covariate causing a delay in failure and thus *increasing* the expected time until failure.

The difficulty that arises with the AFT metric is merely that it places an emphasis on log(time-tofailure) rather than risk (hazard) of failure. With this emphasis usually comes a desire to predict the time to failure, and therein lies the difficulty with complex survival data. Predicting the log(time to failure) with predict assumes that the subject is at risk from time 0 until failure and has a fixed covariate pattern over this period. With these data, such assumptions produce predictions having little to do with the test subjects, who exhibit not only time-varying covariates but also multiple failures.

Predicting time to failure with complex survival data is difficult regardless of the metric under which estimation took place. Those who estimate in the PH metric are probably used to dealing with results from Cox regression, of which predicted time to failure is typically not the focus.

Example 5

The multiple-failure data above are close enough to exponentially distributed that we will reestimate using exponential regression:

| . streg x1 x2 | , d(exp) vce(| robust) | | | | | |
|----------------|---------------|--------------|------------|------------|----------|-------|-----------|
| Iteration 0: | log pseudol: | ikelihood = | -1398.25 | 04 | | | |
| Iteration 1: | log pseudol: | ikelihood = | -1343.60 | 33 | | | |
| Iteration 2: | log pseudol: | ikelihood = | -1341.593 | 32 | | | |
| Iteration 3: | log pseudol: | ikelihood = | -1341.589 | 93 | | | |
| Iteration 4: | log pseudol: | ikelihood = | -1341.589 | 93 | | | |
| Exponential re | egression 1 | log relative | e-hazard : | form | | | |
| No. of subject | ts = | 926 | | Numbe | r of obs | = | 1734 |
| No. of failure | es = | 808 | | | | | |
| Time at risk | = | 435444 | | | | | |
| | | | | Wald | chi2(2) | = | 166.92 |
| Log pseudolike | elihood = -: | 1341.5893 | | Prob | > chi2 | = | 0.0000 |
| • • | | (St | d. Err. a | adjusted f | or 926 c | luste | rs in id) |
| | r | | | J | | | |
| | | Robust | | | | | |
| _t | Haz. Ratio | Std. Err. | z | P> z | [95% C | onf. | Interval] |
| | | | | | | | |
| x1 | 2.19065 | .1684399 | 10.20 | 0.000 | 1.8841 | 86 | 2.54696 |
| x2 | .3037259 | .0462489 | -7.83 | 0.000 | .22535 | 52 | .4093511 |
| _cons | .0024536 | .0001535 | -96.05 | 0.000 | .00217 | 04 | .0027738 |
| | 1 | | | | | | |

Technical note

For our "complex" survival data, we specified vce(robust) when fitting the Weibull and exponential models. This was because these data were stset with an id() variable, and given the time-varying covariates and multiple failures, it is important not to assume that the observations within each subject are independent. When we specified vce(robust), it was implicit that we were "clustering" on the groups defined by the id() variable.

You might sometimes have multiple observations per subject, which exist merely as a result of the data-organization mechanism and are not used to record gaps, time-varying covariates, or multiple failures. Such data could be collapsed into single-observation-per-subject data with no loss of information. In these cases, we refer to splitting the observations to form multiple observations per subject as *noninformative*. When the episode-splitting is noninformative, the model-based (nonrobust) standard errors produced will be the same as those produced when the data are collapsed into single records per subject. Thus, for these type of data, clustering of these multiple observations that results from specifying vce(robust) is not critical.

4

Example 6

A reasonable question to ask is, "Given that we have several possible parametric models, how can we select one?" When parametric models are nested, the likelihood-ratio or Wald test can be used to discriminate between them. This can certainly be done for Weibull versus exponential or gamma versus Weibull or lognormal. When models are not nested, however, these tests are inappropriate, and the task of discriminating between models becomes more difficult. A common approach to this problem is to use the Akaike information criterion (AIC). Akaike (1974) proposed penalizing each log likelihood to reflect the number of parameters being estimated in a particular model and then comparing them. Here the AIC can be defined as

$$AIC = -2(log likelihood) + 2(c + p + 1)$$

where c is the number of model covariates and p is the number of model-specific ancillary parameters listed in table 1. Although the best-fitting model is the one with the largest log likelihood, the preferred model is the one with the smallest AIC value. The AIC value may be obtained by using the estat ic postestimation command; see [R] estat ic.

Using cancer.dta distributed with Stata, let's first fit a generalized gamma model and test the hypothesis that $\kappa = 0$ (test for the appropriateness of the lognormal) and then test the hypothesis that $\kappa = 1$ (test for the appropriateness of the Weibull).

```
. use http://www.stata-press.com/data/r13/cancer
(Patient Survival in Drug Trial)
. stset studytime, failure(died)
 (output omitted)
. replace drug = drug==2 | drug==3 // 0, placebo : 1, nonplacebo
(48 real changes made)
. streg drug age, d(gamma) nolog
         failure _d: died
   analysis time _t: studytime
Gamma regression -- accelerated failure-time form
No. of subjects =
                             48
                                                      Number of obs
                                                                                48
                                                                      =
No. of failures =
                             31
Time at risk
                            744
                                                     LR chi2(2)
                                                                             36.07
                                                                       =
Log likelihood =
                     -42.452006
                                                      Prob > chi2
                                                                       =
                                                                            0.0000
                     Coef.
                             Std. Err.
                                                  P>|z|
                                                             [95% Conf. Interval]
          _t
                                             7.
        drug
                  1.394658
                             .2557198
                                           5.45
                                                  0.000
                                                              .893456
                                                                          1.895859
                 -.0780416
                             .0227978
                                          -3.42
                                                  0.001
                                                            -.1227245
                                                                         -.0333587
         age
       _cons
                  6.456091
                             1.238457
                                           5.21
                                                  0.000
                                                              4.02876
                                                                          8.883421
                 -.3793632
                              .183707
                                          -2.07
                                                  0.039
                                                            -.7394222
                                                                         -.0193041
     /ln_sig
      /kappa
                  .4669252
                             .5419478
                                           0.86
                                                  0.389
                                                             -.595273
                                                                          1.529123
       sigma
                   .684297
                              .1257101
                                                             .4773897
                                                                           .980881
```

The Wald test of the hypothesis that $\kappa = 0$ (test for the appropriateness of the lognormal) is reported in the output above. The *p*-value is 0.389, suggesting that lognormal might be an adequate model for these data.

The Wald test for $\kappa = 1$ is

providing some support against rejecting the Weibull model.

We now fit the exponential, Weibull, loglogistic, and lognormal models separately. To directly compare coefficients, we will ask Stata to report the exponential and Weibull models in AFT form by specifying the time option. The output from fitting these models and the results from the generalized gamma model are summarized in table 2.

| | | | | | Generalized |
|----------------|-------------|------------|------------|-------------|-------------|
| Parameter | Exponential | Weibull | Lognormal | Loglogistic | gamma |
| Age | 0886715 | 0714323 | 0833996 | 0803289 | 078042 |
| Drug | 1.682625 | 1.305563 | 1.445838 | 1.420237 | 1.394658 |
| Constant | 7.146218 | 6.289679 | 6.580887 | 6.446711 | 6.456091 |
| Ancillary | | 1.682751 | 0.751136 | 0.429276 | 0.684297 |
| Kappa | | | | | 0.466925 |
| Log likelihood | -48.397094 | -42.931335 | -42.800864 | -43.21698 | -42.452006 |
| AIC | 102.7942 | 93.86267 | 93.60173 | 94.43396 | 94.90401 |
| | | | | | |

Table 2. Results obtained from streg, using cancer.dta with drug as an indicator variable

The largest log likelihood was obtained for the generalized gamma model; however, the lognormal model is preferred by the AIC.

4

Parameterization of ancillary parameters

By default, all ancillary parameters are estimated as being constant. For example, the ancillary parameter, p, of the Weibull distribution is assumed to be a constant that is not dependent on any covariates. streg's ancillary() and anc2() options allow for complete parameterization of parametric survival models. By specifying, for example,

. streg x1 x2, d(weibull) ancillary(x2 z1 z2)

both λ and the ancillary parameter, p, are parameterized in terms of covariates.

Ancillary parameters are usually restricted to be strictly positive, in which case the logarithm of the ancillary parameter is modeled using a linear predictor, which can assume any value on the real line.

Example 7

Consider a dataset in which we model the time until hip fracture as Weibull for patients on the basis of age, sex, and whether the patient wears a hip-protective device (variable protect). We believe that the hazard is scaled according to sex and the presence of the device but believe the hazards for both sexes to be of different *shapes*.

| . use http://w (hip fracture | - | ss.com/data/ | r13/hip3, | clear | | |
|--|--|-------------------|-----------|-------|-------------|-----------|
| . streg prote | ct age, d(weik | oull) ancill | ary(male) | nolog | | |
| | ure _d: fract ime _t: time1 id: id | | | | | |
| Weibull regres | ssion log 1 | celative-haz | ard form | | | |
| No. of subject No. of failure Time at risk | es = | 148 37 1703 | | Numb | er of obs = | 206 |
| | | | | LR c | :hi2(2) = | 39.80 |
| Log likelihood | d = -69.323 | 3532 | | Prob | > chi2 = | 0.0000 |
| t | Coef. | Std. Err. | z | P> z | [95% Conf. | Interval] |
| _t | | | | | | |
| protect | -2.130058 | .3567005 | -5.97 | 0.000 | -2.829178 | -1.430938 |
| age | .0939131 | .0341107 | 2.75 | 0.006 | .0270573 | .1607689 |
| _cons | -10.17575 | 2.551821 | -3.99 | 0.000 | -15.17722 | -5.174269 |
| ln_p | | | | | | |
| male | 4887189 | .185608 | -2.63 | 0.008 | 8525039 | 1249339 |
| _cons | .4540139 | .1157915 | 3.92 | 0.000 | .2270667 | .6809611 |

From our estimation results, we see that $\ln(p) = 0.454$ for females and $\ln(p) = 0.454 - 0.489 = -0.035$ for males. Thus $\hat{p} = 1.57$ for females and $\hat{p} = 0.97$ for males. When we combine this with the main equation in the model, the estimated hazards are then

$$\hat{h}(t_j|\mathbf{x}_j) = \begin{cases} \exp\left(-10.18 - 2.13 \text{protect}_j + 0.09 \text{age}_j\right) 1.57 t_j^{0.57} & \text{if female} \\ \exp\left(-10.18 - 2.13 \text{protect}_j + 0.09 \text{age}_j\right) 0.97 t_j^{-0.03} & \text{if male} \end{cases}$$

If we believe this model, we would say that the hazard for males given age and protect is almost constant over time.

Contrast this with what we obtain if we type

. streg protect age if male, d(weibull)

. streg protect age if !male, d(weibull)

which is completely general, because not only will the shape parameter, p, differ over both sexes, but the regression coefficients will as well.

4

The anc2() option is for use only with the gamma regression model, because it contains two ancillary parameters—anc2() is used to parametrize κ .

Stratified estimation

When we type

. streg xvars, d(distname) strata(varname)

we are asking that a completely stratified model be fit. By *completely stratified*, we mean that both the model's intercept and any ancillary parameters are allowed to vary for each level of the strata variable. That is, we are constraining the coefficients on the covariates to be the same across strata but allowing the intercept and ancillary parameters to vary.

Example 8

We demonstrate this by fitting a stratified lognormal model to the cancer data, with the drug variable left in its original state: drug==1 refers to the placebo, and drug==2 and drug==3 correspond to two alternative treatments.

| . use http://w (Patient Survi | - | | r13/cance | r | | |
|--|-------------------------------|-----------------|-----------|-------|-------------|-----------|
| . stset studyt (output omitted | | (died) | | | | |
| . streg age, d | d(weibull) st | rata(drug) n | olog | | | |
| | ure _d: died ime _t: study | ytime | | | | |
| Weibull regres | ssion log n | relative-haz | ard form | | | |
| No. of subject No. of failure Time at risk | | 48 31 744 | | Numb | er of obs = | 48 |
| | | | | LR c | hi2(3) = | 16.58 |
| Log likelihood | d = -41.113 | 3074 | | Prob | > chi2 = | 0.0009 |
| t | Coef. | Std. Err. | Z | P> z | [95% Conf. | Interval] |
| _t | | | | | | |
| age | .1212332 | .0367538 | 3.30 | 0.001 | .049197 | .1932694 |
| _Sdrug_2 | -4.561178 | 2.339448 | -1.95 | 0.051 | -9.146411 | .0240556 |
| _Sdrug_3 | -3.715737 | 2.595986 | -1.43 | 0.152 | -8.803776 | 1.372302 |
| _cons | -10.36921 | 2.341022 | -4.43 | 0.000 | -14.95753 | -5.780896 |
| ln_p | | | | | | |
| r Sdrug_2 | .4872195 | .332019 | 1.47 | 0.142 | 1635257 | 1.137965 |
| _Sdrug_3 | .2194213 | .4079989 | 0.54 | 0.591 | 5802418 | 1.019084 |
| _cons | .4541282 | .1715663 | 2.65 | 0.008 | .1178645 | .7903919 |
| | | | | | | |

Completely stratified models are fit by first generating stratum-specific indicator variables (dummy variables) and then adding these as independent variables in the model and as covariates in the ancillary parameter. The strata() option is thus merely a shorthand method for generating the indicator variables from the drug categories and then placing these indicators in *both* the main equation and the ancillary equation(s).

We associate the term *stratification* with this process by noting that the intercept term of the main equation is a component of the baseline hazard (or baseline survivor) function. By allowing this intercept, as well as the ancillary shape parameter, to vary with respect to the strata, we allow the baseline functions to completely vary over the strata, analogous to a stratified Cox model.

4

Example 9

We can produce a less-stratified model by specifying a factor variable in the ancillary() option.

```
. streg age, d(weibull) ancillary(i.drug) nolog
         failure _d:
                       died
   analysis time _t: studytime
Weibull regression -- log relative-hazard form
No. of subjects =
                              48
                                                      Number of obs
                                                                                 48
                                                                       _
No. of failures =
                              31
Time at risk
                             744
                                                      LR chi2(1)
                                                                               9.61
Log likelihood =
                     -44.596379
                                                      Prob > chi2
                                                                             0.0019
                                                                       _
                     Coef.
                              Std. Err.
                                                   P>|z|
                                                              [95% Conf. Interval]
          _t
                                              z
_t
                              .0362786
                                                   0.002
                                                                           .1837466
                  .1126419
                                           3.10
                                                              .0415373
         age
                                                   0.000
       _cons
                 -10.95772
                              2.308489
                                          -4.75
                                                             -15.48227
                                                                         -6.433162
ln_p
        drug
          2
                 -.3279568
                                .11238
                                          -2.92
                                                   0.004
                                                             -.5482176
                                                                           -.107696
          3
                 -.4775351
                              .1091141
                                          -4.38
                                                   0.000
                                                             -.6913948
                                                                          -.2636755
                  .6684086
                              .1327284
                                            5.04
                                                   0.000
                                                              .4082657
                                                                           .9285514
       _cons
```

By doing this, we are restricting not only the coefficients on the covariates to be the same across "strata" but also the intercept, while allowing only the ancillary parameter to differ.

By using ancillary() or strata(), we may thus consider a wide variety of models, depending on what we believe about the effect of the covariate(s) in question. For example, when fitting a Weibull PH model to the cancer data, we may choose from many models, depending on what we want to assume is the effect of the categorical variable drug. For all models considered below, we assume implicitly that the effect of age is proportional on the hazard function.

1. drug has no effect:

```
. streg age, d(weibull)
```

2. The effect of drug is proportional on the hazard (scale), and the effect of age is the same for each level of drug:

. streg age i.drug, d(weibull)

3. drug affects the shape of the hazard, and the effect of age is the same for each level of drug:

. streg age, d(weibull) ancillary(i.drug)

4. drug affects both the scale and shape of the hazard, and the effect of age is the same for each level of drug:

. streg age, d(weibull) strata(drug)

5. drug affects both the scale and shape of the hazard, and the effect of age is different for each level of drug:

4

. streg drug##c.age, d(weibull) strata(drug)

These models may be compared using Wald or likelihood-ratio tests when the models in question are nested (such as 3 nested within 4) or by using the AIC for nonnested models.

Everything we said regarding the modeling of ancillary parameters and stratification applies to AFT models as well, for which interpretations may be stated in terms of the baseline survivor function, that is, the unaccelerated probability of survival past time t.

Technical note

When fitting PH models, streg will, by default, display the exponentiated regression coefficients, labeled as hazard ratios. However, in our previous examples using ancillary() and strata(), the regression outputs displayed the untransformed coefficients instead. This change in behavior has to do with the modeling of the ancillary parameter. When we use one or more covariates from the main equation to model an ancillary parameter, hazard ratios (and time ratios for AFT models) lose their interpretation. streg, as a precaution, disallows the display of hazard/time ratios when ancillary(), anc2(), or strata() is specified.

Keep this in mind when comparing results across various model specifications. For example, when comparing a stratified Weibull PH model to a standard Weibull PH model, be sure that the latter is displayed using the nohr option.

(Unshared-) frailty models

A frailty model is a survival model with unobservable heterogeneity, or *frailty*. At the observation level, frailty is introduced as an unobservable multiplicative effect, α , on the hazard function, such that

$$h(t|\alpha) = \alpha h(t)$$

where h(t) is a nonfrailty hazard function, say, the hazard function of any of the six parametric models supported by streg described earlier in this entry. The frailty, α , is a random positive quantity and, for model identifiability, is assumed to have mean 1 and variance θ .

Exploiting the relationship between the cumulative hazard function and survivor function yields the expression for the survivor function, given the frailty

$$S(t|\alpha) = \exp\left\{-\int_0^t h(u|\alpha)du\right\} = \exp\left\{-\alpha\int_0^t \frac{f(u)}{S(u)}du\right\} = \{S(t)\}^\alpha$$

where S(t) is the survivor function that corresponds to h(t).

Because α is unobservable, it must be integrated out of $S(t|\alpha)$ to obtain the unconditional survivor function. Let $g(\alpha)$ be the probability density function of α , in which case an estimable form of our frailty model is achieved as

$$S_{\theta}(t) = \int_{0}^{\infty} S(t|\alpha)g(\alpha)d\alpha = \int_{0}^{\infty} \left\{S(t)\right\}^{\alpha} g(\alpha)d\alpha$$

Given the unconditional survivor function, we can obtain the unconditional hazard and density in the usual way:

$$f_{\theta}(t) = -\frac{d}{dt}S_{\theta}(t) \qquad h_{\theta}(t) = \frac{f_{\theta}(t)}{S_{\theta}(t)}$$

Hence, an unshared-frailty model is merely a typical parametric survival model, with the additional estimation of an overdispersion parameter, θ . In a standard survival regression, the likelihood calculations are based on S(t), h(t), and f(t). In an unshared-frailty model, the likelihood is based analogously on $S_{\theta}(t)$, $h_{\theta}(t)$, and $f_{\theta}(t)$.

At this stage, the only missing piece is the choice of frailty distribution, $g(\alpha)$. In theory, any continuous distribution supported on the positive numbers that has expectation 1 and finite variance θ is allowed here. For mathematical tractability, however, we limit the choice to either the gamma $(1/\theta, \theta)$ distribution or the inverse-Gaussian distribution with parameters 1 and $1/\theta$, denoted as IG $(1, 1/\theta)$. The gamma(a, b) distribution has probability density function

$$g(x) = \frac{x^{a-1}e^{-x/b}}{\Gamma(a)b^a}$$

and the IG(a, b) distribution has density

$$g(x) = \left(\frac{b}{2\pi x^3}\right)^{1/2} \exp\left\{-\frac{b}{2a}\left(\frac{x}{a} - 2 + \frac{a}{x}\right)\right\}$$

Therefore, performing the integrations described above will show that specifying frailty(gamma) will result in the frailty survival model (in terms of the nonfrailty survivor function, S(t))

$$S_{\theta}(t) = [1 - \theta \log \{S(t)\}]^{-1/\theta}$$

Specifying frailty(invgaussian) will give

$$S_{\theta}(t) = \exp\left\{\frac{1}{\theta} \left(1 - \left[1 - 2\theta \log\left\{S(t)\right\}\right]^{1/2}\right)\right\}$$

Regardless of the choice of frailty distribution, $\lim_{\theta \to 0} S_{\theta}(t) = S(t)$, and thus the frailty model reduces to S(t) when there is no heterogeneity present.

When using frailty models, distinguish between the hazard faced by the individual (subject), $\alpha h(t)$, and the "average" hazard for the population, $h_{\theta}(t)$. Similarly, an individual will have probability of survival past time t equal to $\{S(t)\}^{\alpha}$, whereas $S_{\theta}(t)$ will measure the proportion of the population surviving past time t. You specify S(t) as before with distribution(distname), and the list of possible parametric forms for S(t) is given in table 1. Thus when you specify distribution() you are specifying a model for an individual with frailty equal to one. Specifying frailty(distname) determines which of the two above forms for $S_{\theta}(t)$ is used.

The output of the estimation remains unchanged from the nonfrailty version, except for the additional estimation of θ and a likelihood-ratio test of H_0 : $\theta = 0$. For more information on frailty models, Hougaard (1986) offers an excellent introduction. For a Stata-specific overview, see Gutierrez (2002).

Example 10

Consider as an example a survival analysis of data on women with breast cancer. Our hypothetical dataset consists of analysis times on 80 women with covariates age, smoking, and dietfat, which measures the average weekly calories from fat $(\times 10^3)$ in the patient's diet over the course of the study.

- . use http://www.stata-press.com/data/r13/bc
- . list in 1/12

| | age | smoking | dietfat | t | dead |
|-----|-----|---------|---------|------|------|
| 1. | 30 | 1 | 4.919 | 14.2 | 0 |
| 2. | 50 | 0 | 4.437 | 8.21 | 1 |
| з. | 47 | 0 | 5.85 | 5.64 | 1 |
| 4. | 49 | 1 | 5.149 | 4.42 | 1 |
| 5. | 52 | 1 | 4.363 | 2.81 | 1 |
| 6. | 29 | 0 | 6.153 | 35 | 0 |
| 7. | 49 | 1 | 3.82 | 4.57 | 1 |
| 8. | 27 | 1 | 5.294 | 35 | 0 |
| 9. | 47 | 0 | 6.102 | 3.74 | 1 |
| 10. | 59 | 0 | 4.446 | 2.29 | 1 |
| 11. | 35 | 0 | 6.203 | 15.3 | 0 |
| 12. | 26 | 0 | 4.515 | 35 | 0 |

The data are well fit by a Weibull model for the distribution of survival time conditional on age, smoking, and dietary fat. By omitting the dietfat variable from the model, we hope to introduce unobserved heterogeneity.

```
. stset t, fail(dead)
 (output omitted)
. streg age smoking, d(weibull) frailty(gamma)
         failure _d: dead
   analysis time _t: t
Fitting Weibull model:
Fitting constant-only model:
Iteration 0:
               \log likelihood = -137.15363
Iteration 1:
               log likelihood = -136.3927
Iteration 2:
               log likelihood = -136.01557
Iteration 3:
               \log likelihood = -136.01202
Iteration 4:
               log likelihood = -136.01201
Fitting full model:
Iteration 0:
               log likelihood = -85.933969
Iteration 1:
               log likelihood = -73.61173
Iteration 2:
               \log likelihood = -68.999447
Iteration 3:
               \log likelihood = -68.340858
Iteration 4:
               \log likelihood = -68.136187
Iteration 5:
               \log likelihood = -68.135804
Iteration 6:
               log likelihood = -68.135804
```

| Weibull regre | - | relative-haz a frailty | aru ioim | | | | |
|---|---|--|---|--|---|-------------|--|
| No. of subject | ts = | 80 | | Numb | er of obs | = | 80 |
| No. of failur | | 58 | | | | | |
| Time at risk | | 7.07 | | | | | |
| | | | | LR c | hi2(2) | = | 135.75 |
| Log likelihoo | d = -68.13 | 5804 | | Prob | > chi2 | = | 0.000 |
| t | Haz. Ratio | Std. Err. | Z | P> z | [95% Con: | f. 1 | [nterval] |
| age | 1.475948 | .1379987 | 4.16 | 0.000 | 1.228811 | | 1.772788 |
| smoking | 2.788548 | 1.457031 | 1.96 | 0.050 | 1.00143 | | 7.764894 |
| _cons | 4.57e-11 | 2.38e-10 | -4.57 | 0.000 | 1.70e-15 | | 1.23e-06 |
| /ln_p | 1.087761 | .222261 | 4.89 | 0.000 | .6521376 | | 1.523385 |
| /ln_the | .3307466 | .5250758 | 0.63 | 0.529 | 698383 | | 1.359876 |
| p | 2.967622 | .6595867 | | | 1.91964 | | 4.587727 |
| 1/p | .3369701 | .0748953 | | | .2179729 | | .520931 |
| theta | 1.392007 | .7309092 | | | .4973889 | | 3.895711 |
| Likelihood-ra e could also us . streg age sm failu | e an inverse-C moking, d(weil | Gaussian distr bull) frailt | ribution t | o model t | • | | |
| e could also us . streg age si | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : | Gaussian distr bull) frailt relative-haz | ribution to y(invgaus ard form | o model t | he heteroger | | |
| e could also us . streg age su failu analysis t: Weibull regres | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve | Gaussian distr bull) frailt relative-haz rse-Gaussian | ribution to y(invgaus ard form | o model t ss) nolog | he heteroger | | y. |
| e could also us . streg age su failu analysis t Weibull regres No. of subjec | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve: ts = | Gaussian distr bull) frailt relative-haz rse-Gaussian 80 | ribution to y(invgaus ard form | o model t ss) nolog | he heteroger | neit | y. |
| e could also us . streg age su failu analysis t: Weibull regres No. of subject No. of failure | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve: ts = es = | Gaussian distr bull) frailt relative-haz rse-Gaussian 80 58 | ribution to y(invgaus ard form | o model t ss) nolog | he heteroger | neit | y. |
| e could also us . streg age su failu analysis t: Weibull regres No. of subject | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve: ts = es = | Gaussian distr bull) frailt relative-haz rse-Gaussian 80 | ribution to y(invgaus ard form | o model t ss) nolog Numb | he heteroger er of obs | = | y. 80 |
| e could also us . streg age su failu analysis t: Weibull regres No. of subject No. of failure | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve: ts = es = = 125 | Gaussian distr bull) frailt relative-haz rse-Gaussian 80 58 7.07 | ribution to y(invgaus ard form | o model t ss) nolog Numb LR c | he heteroger | neit | y. 80 125.44 |
| e could also us . streg age su fail analysis t: Weibull regres No. of subjec No. of failur Time at risk | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve: ts = es = = 125 | Gaussian distr bull) frailt relative-haz rse-Gaussian 80 58 7.07 | ribution to y(invgaus ard form | o model t ss) nolog Numb LR c | he heteroger er of obs hi2(2) | = = = | y. 80 125.44 0.0000 |
| e could also us . streg age su fail analysis t: Weibull regres No. of subjec No. of failur Time at risk Log likelihood | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve: ts = es = = 125 d = -73.834 | Gaussian distr bull) frailt relative-haz rse-Gaussian 80 58 7.07 8578 | ribution t y(invgaus ard form frailty | o model t ss) nolog Numb LR c Prob | he heteroger er of obs hi2(2) > chi2 | = = = | y. 80 125.44 0.0000 |
| e could also us . streg age su failu analysis t: Weibull regree No. of subject No. of failure Time at risk Log likelihood t age | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve: ts = es = = 125 d = -73.833 Haz. Ratio | Gaussian distr bull) frailt relative-haz rse-Gaussian 80 58 7.07 8578 Std. Err. | ribution to y(invgaus ard form frailty z | o model t ss) nolog Numb LR c Prob | he heteroger er of obs hi2(2) > chi2 [95% Con: | = = = | y. 125.44 0.0000 [Interval] 1.378215 |
| e could also us . streg age su failu analysis t: Weibull regres No. of subjec: No. of failur Time at risk Log likelihood | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve: ts = es = = 125 d = -73.833 Haz. Ratio 1.284133 | Gaussian distr bull) frailt relative-haz rse-Gaussian 80 58 7.07 8578 Std. Err. .0463256 | ribution to y(invgause ard form frailty z 6.93 | o model t ss) nolog Numb LR c Prob P> z 0.000 | he heteroger er of obs hi2(2) > chi2 [95% Con: 1.196473 | = = = | y. 125.44 0.0000 [Interval] 1.378217 6.764528 |
| e could also us . streg age sm failm analysis t: Weibull regree No. of subject No. of failure Time at risk Log likelihood t age smoking | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve ts = es = = 125" d = -73.834 Haz. Ratio 1.284133 2.905409 | Gaussian distr bull) frailt relative-haz rse-Gaussian 80 58 7.07 8578 Std. Err. .0463256 1.252785 | ribution to y(invgause ard form frailty z 6.93 2.47 | o model t ss) nolog Numb LR c: Prob P> z 0.000 0.013 | he heteroger er of obs hi2(2) > chi2 [95% Con: 1.196473 1.247892 | = = = | y. 125.44 0.0000 [nterval] 1.378217 6.764528 6.79e-06 |
| e could also us . streg age su failu analysis t: Weibull regree No. of subjec: No. of failury Time at risk Log likelihood | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve: ts = es = = 125 d = -73.83 Haz. Ratio 1.284133 2.905409 1.11e-07 | Gaussian distr bull) frailt relative-haz rse-Gaussian 80 58 7.07 8578 Std. Err. .0463256 1.252785 2.34e-07 | ribution to y(invgause ard form frailty z 6.93 2.47 -7.63 | o model t ss) nolog Numb LR c: Prob P> z 0.000 0.013 0.000 | he heteroger er of obs hi2(2) > chi2 [95% Con: 1.196473 1.247892 1.83e-09 | = = = | y. 80 125.44 0.0000 |
| e could also us . streg age su failu analysis t: Weibull regres No. of subjec: No. of failur Time at risk Log likelihood t age smoking cons /ln_p | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve: ts = es = = 125 d = -73.83 Haz. Ratio 1.284133 2.905409 1.11e-07 .7173904 | Gaussian distribull) frailt relative-haz rse-Gaussian 80 58 7.07 8578 Std. Err. .0463256 1.252785 2.34e-07 .1434382 | ribution to y(invgaus ard form frailty z 6.93 2.47 -7.63 5.00 | o model t ss) nolog Numb LR c: Prob P> z 0.000 0.013 0.000 0.000 | he heterogen er of obs hi2(2) > chi2 [95% Con: 1.196473 1.247892 1.83e-09 .4362567 | = = = | y. 125.44 0.0000 [nterval] 1.378217 6.764528 6.79e-06 .9985241 |
| e could also us . streg age su failu analysis t: Weibull regress No. of subject No. of failure Time at risk Log likelihood t age smoking cons /ln_p /ln_the | e an inverse-C moking, d(weil ure _d: dead ime _t: t ssion log : Inve: ts = es = = 125 d = -73.833 Haz. Ratio 1.284133 2.905409 1.11e-07 .7173904 .2374778 | Gaussian distribull) frailt relative-haz rse-Gaussian 80 58 7.07 8578 Std. Err. .0463256 1.252785 2.34e-07 .1434382 .8568064 | ribution to y(invgaus ard form frailty z 6.93 2.47 -7.63 5.00 | o model t ss) nolog Numb LR c: Prob P> z 0.000 0.013 0.000 0.000 | he heterogen er of obs hi2(2) > chi2 [95% Con: 1.196473 1.247892 1.83e-09 .4362567 -1.441832 | = = = | y. 125.4 0.0000 [nterval] 1.37821 6.764523 6.79e-00 .998524 1.916783 |

Likelihood-ratio test of theta=0: chibar2(01) = 11.16 Prob>=chibar2 = 0.000

1.086471

theta

1.268047

The results are similar with respect to the choice of frailty distribution, with the gamma frailty model producing a slightly higher likelihood. Both models show a statistically significant level of unobservable heterogeneity because the *p*-value for the likelihood-ratio (LR) test of H_0 : $\theta = 0$ is virtually zero in both cases.

.2364941

6.799082

Technical note

With gamma-distributed or inverse-Gaussian-distributed frailty, hazard ratios decay over time in favor of the *frailty effect*, and thus the displayed "Haz. Ratio" in the above output is actually the hazard ratio only for t = 0. The degree of decay depends on θ . Should the estimated θ be close to zero, the hazard ratios regain their usual interpretation. The rate of decay and the limiting hazard ratio differ between the gamma and inverse-Gaussian models; see Gutierrez (2002) for details.

For this reason, many researchers prefer fitting frailty models in the AFT metric because the interpretation of regression coefficients is unchanged by the frailty—the factors in question serve to either accelerate or decelerate the survival experience. The only difference is that with frailty models, the unconditional probability of survival is described by $S_{\theta}(t)$ rather than S(t).

Technical note

The LR test of $\theta = 0$ is a boundary test and thus requires careful consideration concerning the calculation of its *p*-value. In particular, the null distribution of the LR test statistic is not the usual χ_1^2 but rather is a 50:50 mixture of a χ_0^2 (point mass at zero) and a χ_1^2 , denoted as $\bar{\chi}_{01}^2$. See Gutierrez, Carter, and Drukker (2001) for more details.

To verify that the significant heterogeneity is caused by the omission of dietfat, we now refit the Weibull/inverse-Gaussian frailty model with dietfat included.

| . streg age smoking dietfat, d(weibull) frailty(invgauss) nolog | | | | | | |
|---|-------------|------------------------------|-------|--------|------------|-----------|
| failure _d: dead analysis time _t: t | | | | | | |
| · | | | | | | |
| Weibull regres | • | relative-haz rse-Gaussian | | | | |
| No. of subject | ts = | 80 | | Number | c of obs = | 80 |
| No. of failure | es = | 58 | | | | |
| Time at risk | = 1257 | 7.07 | | | | |
| | | | | LR chi | i2(3) = | 246.41 |
| Log likelihood | d = −13.352 | 2142 | | Prob > | > chi2 = | 0.0000 |
| _t | Haz. Ratio | Std. Err. | z | P> z | [95% Conf. | Interval] |
| age | 1.74928 | .0985244 | 9.93 | 0.000 | 1.566453 | 1.953446 |
| smoking | 5.203549 | 1.70494 | 5.03 | 0.000 | 2.737815 | 9.889978 |
| dietfat | 9.229841 | 2.219328 | 9.24 | 0.000 | 5.761315 | 14.78655 |
| _cons | 1.07e-20 | 4.98e-20 | -9.92 | 0.000 | 1.22e-24 | 9.45e-17 |
| /ln_p | 1.431742 | .0978844 | 14.63 | 0.000 | 1.239892 | 1.623592 |
| /ln_the | -14.42565 | 2850.629 | -0.01 | 0.996 | -5601.555 | 5572.704 |
| p | 4.185986 | .4097429 | | | 3.455242 | 5.071275 |
| 1/p | .2388923 | .0233838 | | | .1971891 | .2894153 |
| theta | 5.43e-07 | .0015487 | | | 0 | |
| | | | | | | |

Likelihood-ratio test of theta=0: chibar2(01) = 0.00 Prob>=chibar2 = 1.000

The estimate of the frailty variance component θ is near zero, and the *p*-value of the test of $H_0: \theta = 0$ equals one, indicating negligible heterogeneity. A regular Weibull model could be fit to these data (with dietfat included), producing almost identical estimates of the hazard ratios and ancillary parameter, *p*, so such an analysis is omitted here.

Also hazard ratios now regain their original interpretation. Thus an increase in weekly calories from fat of 1,000 would increase the risk of death by more than ninefold.

4

Shared-frailty models

A generalization of the frailty models considered in the previous section is the *shared-frailty* model, where the frailty is assumed to be group specific; this is analogous to a panel-data regression model. For observation j from the *i*th group, the hazard is

```
h_{ij}(t|\alpha_i) = \alpha_i h_{ij}(t)
```

for i = 1, ..., n and $j = 1, ..., n_i$, where by $h_{ij}(t)$ we mean $h(t|\mathbf{x}_{ij})$, which is the individual hazard given covariates \mathbf{x}_{ij} .

Shared-frailty models are appropriate when you wish to model the frailties as being specific to groups of subjects, such as subjects within families. Here a shared-frailty model may be used to model the degree of correlation within groups; that is, the subjects within a group are correlated because they share the same common frailty.

Example 11

Consider the data from a study of 38 kidney dialysis patients, as described in McGilchrist and Aisbett (1991). The study is concerned with the prevalence of infection at the catheter-insertion point. Two recurrence times (in days) are measured for each patient, and each recorded time is the time from initial insertion (onset of risk) to infection or censoring.

. use http://www.stata-press.com/data/r13/catheter
(Kidney data, McGilchrist and Aisbett, Biometrics, 1991)
. list patient time infect age female in 1/10

| | patient | time | infect | age | female |
|----------|---------|------|--------|------|--------|
| 1. | 1 | 16 | 1 | 28 | 0 |
| 2. | 1 | 8 | 1 | 28 | 0 |
| 2. 3. | 2 | 13 | 0 | 48 | 1 |
| 4. 5. | 2 | 23 | 1 | 48 | 1 |
| 5. | 3 | 22 | 1 | 32 | 0 |
| | | | | | |
| 6. | 3 | 28 | 1 | 32 | 0 |
| 7. 8. | 4 | 318 | 1 | 31.5 | 1 |
| 8. | 4 | 447 | 1 | 31.5 | 1 |
| 9. | 5 | 30 | 1 | 10 | 0 |
| 10. | 5 | 12 | 1 | 10 | 0 |
| | | | | | i |

Each patient (patient) has two recurrence times (time) recorded, with each catheter insertion resulting in either infection (infect==1) or right-censoring (infect==0). Among the covariates measured are age and sex (female==1 if female, female==0 if male).

One subtlety to note concerns the use of the generic term *subjects*. In this example, the subjects are the individual catheter insertions, not the patients themselves. This is a function of how the data were recorded—the onset of risk occurs at catheter insertion (of which there are two for each patient) not, say, at the time of admission of the patient into the study. Thus we have two subjects (insertions) within each group (patient).

It is reasonable to assume independence of patients but unreasonable to assume that recurrence times within each patient are independent. One solution would be to fit a standard survival model, adjusting the standard errors of the parameter estimates to account for the possible correlation by specifying vce(cluster patient).

We could also model the correlation by assuming that the correlation is the result of a latent patient-level effect, or frailty. That is, rather than fitting a standard model and specifying vce(cluster patient), we fit a frailty model and specify shared(patient). Assuming that the time to infection, given age and female, follows a Weibull distribution, and inverse-Gaussian distributed frailties, we get

| . stset time, (output omitted | | | | | | |
|----------------------------------|------------------------------|--------------|-----------|-----------|---------------|-----------|
| . streg age fe | emale, d(weibu | ıll) frailty | (invgauss | s) shared | (patient) nol | og |
| failu analysis ti | ire _d: infe ime _t: time | ct | | | | |
| Weibull regres | ssion | | | | | |
| 0 | relative-haza | | | Number | | 76 |
| Inve Group variable | rse-Gaussian s e: patient | shared frail | ty | Number | of groups = | 38 |
| No. of subject | ts = | 76 | | Obs per | group: min = | 2 |
| No. of failure | es = | 58 | | - | avg = | 2 |
| Time at risk | = | 7424 | | | max = | 2 |
| | | | | LR chi2 | (2) = | 9.84 |
| Log likelihood | d = -99.093 | 3527 | | Prob > | chi2 = | 0.0073 |
| t | Haz. Ratio | Std. Err. | z | P> z | [95% Conf. | Interval] |
| age | 1.006918 | .013574 | 0.51 | 0.609 | .9806623 | 1.033878 |
| female | .2331376 | .1046382 | -3.24 | 0.001 | .0967322 | .5618928 |
| _cons | .0110089 | .0099266 | -5.00 | 0.000 | .0018803 | .0644557 |
| /ln_p | .1900625 | .1315342 | 1.44 | 0.148 | 0677398 | .4478649 |
| /ln_the | .0357272 | .7745362 | 0.05 | 0.963 | -1.482336 | 1.55379 |
| р | 1.209325 | .1590676 | | | .9345036 | 1.564967 |
| 1/p | .8269074 | .1087666 | | | .638991 | 1.070087 |
| theta | 1.036373 | .8027085 | | | .2271066 | 4.729362 |

Likelihood-ratio test of theta=0: chibar2(01) = 8.70 Prob>=chibar2 = 0.002

| . streg age fe | emale, d(lnorr | mal) frailty | (invgauss | s) shared | (patient) nol | Log |
|----------------------|---|--------------|-----------|-----------|---------------|-----------|
| failu analysis ti | ire _d: infec ime _t: time | ct | | | | |
| Lognormal regi | ression | | | | | |
| accel | accelerated failure-time form Number of obs = | | | | = 76 | |
| Inve | rse-Gaussian s | shared frail | ty | Number | of groups = | = 38 |
| Group variable | e: patient | | | | | |
| No. of subject | ts = | 76 | | Obs per | group: min = | = 2 |
| No. of failure | es = | 58 | | - | avg = | = 2 |
| Time at risk | = | 7424 | | | max = | = 2 |
| | | | | LR chi2 | (2) = | = 16.34 |
| Log likelihood | d = -97.614 | 4583 | | Prob > | chi2 = | = 0.0003 |
| | | | | | | |
| _t | Coef. | Std. Err. | z | P> z | [95% Conf. | Interval] |
| age | 0066762 | .0099457 | -0.67 | 0.502 | 0261694 | .0128171 |
| female | 1.401719 | .3334931 | 4.20 | 0.000 | .7480844 | 2.055354 |
| _cons | 3.336709 | .4972641 | 6.71 | 0.000 | 2.362089 | 4.311329 |
| /ln_sig | .0625872 | .1256185 | 0.50 | 0.618 | 1836205 | .3087949 |
| /ln_the | -1.606248 | 1.190775 | -1.35 | 0.177 | -3.940125 | .7276282 |
| sigma | 1.064587 | .1337318 | | | .8322516 | 1.361783 |
| theta | .2006389 | .2389159 | | | .0194458 | 2.070165 |
| | •••••••••••••••••••••••••••••••••••••• | | | | | |

Contrast this with what we obtain by assuming a subject-level lognormal model:

Likelihood-ratio test of theta=0: chibar2(01) = 1.53 Prob>=chibar2 = 0.108

The frailty effect is insignificant at the 10% level in the latter model yet highly significant in the former. We thus have two possible stories to tell concerning these data: If we believe the first model, we believe that the individual hazard of infection continually rises over time (Weibull), but there is a significant frailty effect causing the population hazard to begin falling after some time. If we believe the second model, we believe that the individual hazard first rises and then declines (lognormal), meaning that if a given insertion does not become infected initially, the chances that it will become infected begin to decrease after a certain point. Because the frailty effect is insignificant, the population hazard mirrors the individual hazard in the second model.

As a result, both models view the population hazard as rising initially and then falling past a certain point. The second version of our story corresponds to higher log likelihood, yet perhaps not significantly higher given the limited data. More investigation is required. One idea is to fit a more distribution-agnostic form of a frailty model, such as a piecewise exponential (Cleves et al. 2010, 328–331) or a Cox model with frailty; see [ST] stcox.

4

Shared-frailty models are also appropriate when the frailties are subject specific yet there exist multiple records per subject. Here you would share frailties across the same id() variable previously stset. When you have subject-specific frailties and uninformative episode splitting, it makes no difference whether you fit a shared or an unshared frailty model. The estimation results will be the same.

Stored results

streg stores the following in e():

| and b | |
|---------------|---|
| e(N) | number of observations |
| e(N_sub) | number of subjects |
| e(N_fail) | number of failures |
| e(N_g) | number of groups |
| 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(ll_c) | log likelihood, comparison model |
| e(N_clust) | number of clusters |
| e(chi2) | χ^2 |
| e(chi2_c) | χ^2 , comparison model |
| e(risk) | total time at risk |
| e(g_min) | smallest group size |
| e(g_avg) | average group size |
| e(g_max) | largest group size |
| e(theta) | frailty parameter |
| e(aux_p) | ancillary parameter (weibull) |
| e(gamma) | ancillary parameter (gompertz, loglogistic) |
| e(sigma) | ancillary parameter (gamma, lnormal) |
| e(kappa) | ancillary parameter (gamma) |
| e(p) | significance |
| e(p_c) | significance, comparison model |
| 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 |
| | |

| 1110 | 10103 | |
|------|-----------------|--|
| | e(cmd) | model or regression name |
| | e(cmd2) | streg |
| | e(cmdline) | command as typed |
| | e(dead) | _d |
| | e(depvar) | _t |
| | e(title) | title in estimation output |
| | e(title2) | secondary title in estimation output |
| | e(clustvar) | name of cluster variable |
| | e(shared) | frailty grouping variable |
| | e(fr_title) | title in output identifying frailty |
| | e(wtype) | weight type |
| | e(wexp) | weight expression |
| | e(t0) | _t0 |
| | 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(stcurve) | stcurve |
| | 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(predict) | program used to implement predict |
| | e(predict_sub) | predict subprogram |
| | e(footnote) | program used to implement the footnote display |
| | e(asbalanced) | factor variables fvset as asbalanced |
| | e(asobserved) | factor variables fvset as asobserved |
| Ma | trices | |
| 1010 | 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 |
| Em | nctions | |
| Füi | | marks estimation sample |
| | e(sample) | marks commander sample |

Methods and formulas

Macros

For an introduction to survival models, see Cleves et al. (2010). For an introduction to survival analysis directed at social scientists, see Box-Steffensmeier and Jones (2004).

Consider for j = 1, ..., n observations the trivariate response, (t_{0j}, t_j, d_j) , representing a period of observation, $(t_{0j}, t_j]$, ending in either failure $(d_j = 1)$ or right-censoring $(d_j = 0)$. This structure allows analysis of a wide variety of models and may be used to account for delayed entry, gaps, time-varying covariates, and multiple failures per subject. Regardless of the structure of the data, once they are stset, the data may be treated in a common manner by streg: the stset-created variable _t0 holds the t_{0j} , _t holds the t_j , and _d holds the d_j .

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) = f(t)/S(t). Available forms for S(t) are listed in table 1. For a set of covariates from the *j*th observation, \mathbf{x}_j , define $S_j(t) = S(t|\mathbf{x} = \mathbf{x}_j)$, and similarly define $h_j(t)$ and $f_j(t)$. For example, in a Weibull PH model, $S_j(t) = \exp\{-\exp(\mathbf{x}_j\beta)t^p\}$.

Parameter estimation

In this command, β and the ancillary parameters are estimated via maximum likelihood. A subject known to fail at time t_j contributes to the likelihood function the value of the density at time t_j conditional on the entry time t_{0j} , $f_j(t_j)/S_j(t_{0j})$. A censored observation, known to survive only up to time t_j , contributes $S_j(t_j)/S_j(t_{0j})$, which is the probability of surviving beyond time t_j conditional on the entry time, t_{0j} . The log likelihood is thus given by

$$\log L = \sum_{j=1}^{n} \{ d_j \log f_j(t_j) + (1 - d_j) \log S_j(t_j) - \log S_j(t_{0j}) \}$$

Implicit in the above log-likelihood expression are the regression parameters, β , and the ancillary parameters because both are components of the chosen $S_j(t)$ and its corresponding $f_j(t)$; see table 1. streg reports maximum likelihood estimates of β and of the ancillary parameters (if any for the chosen model). The reported log-likelihood value is $\log L_r = \log L + T$, where $T = \sum \log(t_j)$ is summed over uncensored observations. The adjustment removes the time units from $\log L$. Whether the adjustment is made makes no difference to any test or result since such tests and results depend on differences in log-likelihood functions or their second derivatives, or both.

Specifying ancillary(), anc2(), or strata() will parameterize the ancillary parameter(s) by using the linear predictor, $z_j \alpha_z$, where the covariates, z_j , need not be distinct from x_j . Here streg will report estimates of α_z in addition to estimates of β . The log likelihood here is simply the log likelihood given above, with $z_j \alpha_z$ 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() creates indicator variables for the strata, places these indicators in the main equation, and uses the indicators to parameterize any ancillary parameters that exist for the chosen model.

Unshared-frailty models have a log likelihood of the above form, with $S_{\theta}(t)$ and $f_{\theta}(t)$ substituted for S(t) and f(t), respectively. Equivalently, for gamma-distributed frailties,

$$\log L = \sum_{j=1}^{n} \left[\theta^{-1} \log \left\{ 1 - \theta \log S_j(t_{0j}) \right\} - \left(\theta^{-1} + d_j \right) \log \left\{ 1 - \theta \log S_j(t_j) \right\} + d_j \log h_j(t_j) \right]$$

and for inverse-Gaussian-distributed frailties,

$$\log L = \sum_{j=1}^{n} \left[\theta^{-1} \left\{ 1 - 2\theta \log S_j(t_{0j}) \right\}^{1/2} - \theta^{-1} \left\{ 1 - 2\theta \log S_j(t_j) \right\}^{1/2} + d_j \log h_j(t_j) - \frac{1}{2} d_j \log \left\{ 1 - 2\theta \log S_j(t_j) \right\} \right]$$

In a shared-frailty model, the frailty is common to a group of observations. Thus, to form an unconditional likelihood, the frailties must be integrated out at the group level. The data are organized as i = 1, ..., n groups with the *i*th group comprising $j = 1, ..., n_i$ observations. The log likelihood is the sum of the log-likelihood contributions for each group. Define $D_i = \sum_j d_{ij}$ as the number of failures in the *i*th group. For gamma frailties, the log-likelihood contribution for the *i*th group is

$$\log L_{i} = \sum_{j=1}^{n_{i}} d_{ij} \log h_{ij}(t_{ij}) - (1/\theta + D_{i}) \log \left\{ 1 - \theta \sum_{j=1}^{n_{i}} \log \frac{S_{ij}(t_{ij})}{S_{ij}(t_{0ij})} \right\} + D_{i} \log \theta + \log \Gamma(1/\theta + D_{i}) - \log \Gamma(1/\theta)$$

This formula corresponds to the log-likelihood contribution for multiple-record data. For single-record data, the denominator $S_{ij}(t_{0ij})$ is equal to 1. This formula is not applicable to data with delayed entries or gaps.

For inverse-Gaussian frailties, define

$$C_{i} = \left\{ 1 - 2\theta \sum_{j=1}^{n_{i}} \log \frac{S_{ij}(t_{ij})}{S_{ij}(t_{0ij})} \right\}^{-1/2}$$

The log-likelihood contribution for the *i*th group then becomes

$$\log L_i = \theta^{-1}(1 - C_i^{-1}) + B(\theta C_i, D_i) + \sum_{j=1}^{n_i} d_{ij} \{ \log h_{ij}(t_{ij}) + \log C_i \}$$

The function B(a, b) is related to the modified Bessel function of the third kind, commonly known as the BesselK function; see Wolfram (1999, 767). In particular,

$$B(a,b) = a^{-1} + \frac{1}{2} \left\{ \log\left(\frac{2}{\pi}\right) - \log a \right\} + \log \operatorname{BesselK}\left(\frac{1}{2} - b, a^{-1}\right)$$

For both unshared- and shared-frailty models, estimation of θ takes place jointly with the estimation of β and the ancillary parameters.

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 observations in the dataset represent repeated observations on the same subjects (that is, there are time-varying covariates), the assumption of independence of the observations is highly questionable, meaning that the conventional estimate of variance is not appropriate. We strongly advise that you use the vce(robust) and vce(cluster *clustvar*) options here. (streg knows to specify vce(cluster *clustvar*) if you specify vce(robust).) vce(robust) and vce(cluster *clustvar*) do not apply in shared-frailty models, where the correlation within groups is instead modeled directly.

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

Benjamin Gompertz (1779–1865) came from a Jewish family who left Holland and settled in England. He was self-educated in mathematics and in 1824 was appointed as actuary and head clerk of the Alliance Assurance Company. He carried out pioneer work on the application of differential calculus to actuarial questions, particularly the dependence of mortality on age, and contributed to astronomy and the study of scientific instruments.

Ernst Hjalmar Waloddi Weibull (1887–1979) was a Swedish applied physicist most famous for his work on the statistics of material properties. He worked in Germany and Sweden as an inventor and a consulting engineer, publishing his first paper on the propagation of explosive waves in 1914, thereafter becoming a full professor at the Royal Institute of Technology in 1924. Weibull wrote two important papers, "Investigations into strength properties of brittle materials" and "The phenomenon of rupture in solids", which discussed his ideas about the statistical distributions of material strength. These articles came to the attention of engineers in the late 1930s.

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Also see

- [ST] streg postestimation Postestimation tools for streg
- [ST] stcurve Plot survivor, hazard, cumulative hazard, or cumulative incidence function
- [ST] stcox Cox proportional hazards model
- [ST] stcrreg Competing-risks regression
- [ST] sts Generate, graph, list, and test the survivor and cumulative hazard functions
- [ST] stset Declare data to be survival-time data
- [MI] estimation Estimation commands for use with mi estimate
- [SVY] svy estimation Estimation commands for survey data
- [U] 20 Estimation and postestimation commands