

STATA log file for Time-Varying Covariates (TVC) Duration Model Estimations.

This STATA 8.0 log file reports estimations in which CDER Staff Aggregates and PDUFA variable are assigned to drug-months of review for each drug.

That is, the covariate "CDER Staff" varies not only across drugs but **within** drugs, much as they would in a panel estimation. For technical details on these models, see Trond Petersen, "Fitting parametric survival models with time-dependent covariates," *Applied Statistics*, 1986, 281-288.

Throughout this note, the variable "dynstafc" is the CDER staff variable, in which CDER staff varies both across and within drug reviews.

Also, the result of time-varying covariates estimation is to take a dataset of N drugs and to create a dataset (akin to an asymmetric panel) of $N * t_i$ drug months (where t_i is the number of months that drug i was under review at CDER). This creates a much larger "effective" sample size: generally 25,000 drug-months per estimation (this varies depending on missing data in the right-hand side covariates). To highlight this feature in the estimations below, I have highlighted all such time-varying samples in purple [lavender?].

Estimates for the dynamic CDER staff variable are highlighted in blue [aqua?].

Estimates for the PDUFA indicator variable, measuring the effect of the 1992 user-fee law, are highlighted in green [forest?].

```
-----
log: C:\fdatemp\dyn-stafcder-run20040127.log
log type: text
opened on: 27 Jan 2004, 22:17:35

. set memory 256m

Current memory allocation

      current          memory usage
settable  value      description      (1M = 1024k)
-----
set maxvar    5000    max. variables allowed      1.733M
set memory    256M    max. data space             256.000M
set matsize   400     max. RHS vars in models     1.254M
-----
                                258.987M

. use "C:\fdatemp\drugTVC-111801-diz&post&grps&hrg&time2.dta", clear
```

Log-Normal Estimates with Inverse Gaussian Frailty, Shared Frailties by Primary Indication of NDA Submission

```
. streg dynstaafc, dist(lognormal) frailty(invgaussian) shared(discode)
```

```
failure _d: aprovdum
analysis time _t: acttime
id: drugnum
```

Fitting comparison lnnormal model:

Fitting constant-only model:

```
Iteration 0: log likelihood = -843.46133 (not concave)
Iteration 1: log likelihood = -777.86079
Iteration 2: log likelihood = -770.68823
Iteration 3: log likelihood = -770.64722
Iteration 4: log likelihood = -770.64721
```

Fitting full model:

```
Iteration 0: log likelihood = -781.93002
Iteration 1: log likelihood = -760.13243
Iteration 2: log likelihood = -745.82132
Iteration 3: log likelihood = -745.3259
Iteration 4: log likelihood = -745.32139
Iteration 5: log likelihood = -745.32139
```

Log-normal regression --

```
accelerated failure-time form
Inverse-Gaussian shared frailty
```

```
Number of obs = 30726
Number of groups = 116
```

Group variable: discode

```
No. of subjects = 653
No. of failures = 392
Time at risk = 30392.64662

Obs per group: min = 1
                avg = 264.8793
                max = 6100
```

```
Log likelihood = -745.32139

LR chi2(1) = 50.65
Prob > chi2 = 0.0000
```

_t	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
dynstaafc	-.0012803	.0001795	-7.13	0.000	-.001632	-.0009285
_cons	4.697791	.2677995	17.54	0.000	4.172913	5.222668
/ln_sig	-.181791	.0630678	-2.88	0.004	-.3054016	-.0581803
/ln_the	-.1153007	.3035741	-0.38	0.704	-.710295	.4796936
sigma	.8337756	.0525844			.7368274	.9434799
theta	.8910982	.2705143			.4914992	1.615579

Likelihood-ratio test of theta=0: chibar2(01) = 147.10 Prob>=chibar2 = 0.000

Weibull Models with Gamma Frailty, Shared Frailties by Primary Indication of NDA Submission

NOTE THAT STATA REPORTS WEIBULL MODEL COEFFICIENTS IN TERMS OF HAZARD RATIOS. HENCE A HAZARD RATIO GREATER THAN ONE REPRESENTS AN INCREASED EFFECT UPON THE HAZARD, CORRESPONDING TO A DECREASE IN THE APPROVAL TIME.

```
. streg dynstafc, dist(weibull) frailty(gamma) shared(discode)

      failure _d:  aprovdum
analysis time _t:  acttime
              id:  drugnum
```

Fitting comparison weibull model:

Fitting constant-only model:

```
Iteration 0:  log likelihood = -877.66003
Iteration 1:  log likelihood = -843.54879
Iteration 2:  log likelihood = -831.82383
Iteration 3:  log likelihood = -830.93729
Iteration 4:  log likelihood = -830.93591
Iteration 5:  log likelihood = -830.93591
```

Fitting full model:

```
Iteration 0:  log likelihood = -837.20534
Iteration 1:  log likelihood = -828.86368
Iteration 2:  log likelihood = -828.78945
Iteration 3:  log likelihood = -828.7838
Iteration 4:  log likelihood = -828.78335
Iteration 5:  log likelihood = -828.78332
```

Weibull regression --

```
      log-relative hazard form      Number of obs      =      30726
      Gamma shared frailty          Number of groups   =      116
Group variable: discode
```

```
No. of subjects =      653      Obs per group: min =      1
No. of failures =      392      avg = 264.8793
Time at risk    = 30392.64662    max =      6100
```

```
LR chi2(1)      =      4.31
Log likelihood  = -828.78332    Prob > chi2     =      0.0380
```

	_t	Haz. Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
	dynstafc	1.000444	.0002062	2.15	0.031	1.00004 1.000848
	/ln_p	.0320667	.0422953	0.76	0.448	-.0508307 .114964
	/ln_the	-.6969231	.2056806	-3.39	0.001	-1.10005 -.2937965
	p	1.032586	.0436736			.9504396 1.121833
	1/p	.968442	.0409606			.8913982 1.052145
	theta	.4981156	.1024527			.3328545 .7454282

Likelihood-ratio test of theta=0: chibar2(01) = 154.59 Prob>=chibar2 = 0.000

Weibull Model (same as previous) adding static and time-varying year of submission, and order-of-entry variable.

```
. streg dynstafc dynyear subyear orderent, dist(weibull) frailty(gamma) shared(
> discode)
```

```
failure _d: aprovdum
analysis time _t: acttime
id: drugnum
```

Fitting comparison weibull model:

Fitting constant-only model:

```
Iteration 0: log likelihood = -818.54959
Iteration 1: log likelihood = -788.10053
Iteration 2: log likelihood = -773.58715
Iteration 3: log likelihood = -769.16236
Iteration 4: log likelihood = -769.15705
Iteration 5: log likelihood = -769.15705
```

Fitting full model:

```
Iteration 0: log likelihood = -666.0344
Iteration 1: log likelihood = -662.17382
Iteration 2: log likelihood = -651.89997
Iteration 3: log likelihood = -645.71384
Iteration 4: log likelihood = -642.96835
Iteration 5: log likelihood = -642.76086
Iteration 6: log likelihood = -642.7231
Iteration 7: log likelihood = -642.71024
Iteration 8: log likelihood = -642.70536
Iteration 9: log likelihood = -642.70349
Iteration 10: log likelihood = -642.70272
Iteration 11: log likelihood = -642.70237
Iteration 12: log likelihood = -642.70219
Iteration 13: log likelihood = -642.7021
Iteration 14: log likelihood = -642.70205
```

Weibull regression --

```
log-relative hazard form      Number of obs      =      27236
Gamma shared frailty          Number of groups   =      116
Group variable: discode
```

```
No. of subjects =      584      Obs per group: min =      1
No. of failures =      376      avg =    234.7931
Time at risk    =    26936.25207  max =      6100
```

```
Log likelihood =    -642.70205      LR chi2(4)          =      252.91
                                      Prob > chi2         =      0.0000
```

	_t	Haz. Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
dynstafc		1.00157	.0006476	2.43	0.015	1.000301 1.00284
dynyear		.5267652	.0221816	-15.22	0.000	.4850358 .5720847
subyear		1.949885	.0615344	21.16	0.000	1.832933 2.074298
orderent		.979911	.0104373	-1.91	0.057	.9596663 1.000583
/ln_p		.8502338	.0315349	26.96	0.000	.7884264 .9120411
/ln_the		-.9698966	.2706042	-3.58	0.000	-1.500271 -.4395221

p	2.340194	.0737979	2.199932	2.489398
1/p	.427315	.0134754	.4017035	.4545595
theta	.3791222	.1025921	.2230697	.6443443

Likelihood-ratio test of theta=0: chibar2(01) = 54.62 Prob>=chibar2 = 0.000

Add Indicator Variable for PDUFA Change (equals "1" after 1992, "0" before). This is also time-varying (within drug submissions as well as across them).

```
. sum dynpdufa
```

Variable	Obs	Mean	Std. Dev.	Min	Max
dynpdufa	30726	34.94405	46.98424	0	148.4133

```
. gen dyn_pdufadum = 0
```

```
. replace dyn_pdufadum = 1 if(dynpdufa > 0)
(18116 real changes made)
```

```
. streg dynstafc dyn_pdufadum, dist(lognormal) frailty(invgaussian) shared(disc
> ode)
```

```
failure _d: aprovdum
analysis time _t: acttime
id: drugnum
```

Fitting comparison lnnormal model:

Fitting constant-only model:

```
Iteration 0: log likelihood = -843.46133 (not concave)
Iteration 1: log likelihood = -777.86079
Iteration 2: log likelihood = -770.68823
Iteration 3: log likelihood = -770.64722
Iteration 4: log likelihood = -770.64721
```

Fitting full model:

```
Iteration 0: log likelihood = -781.23898
Iteration 1: log likelihood = -758.40019
Iteration 2: log likelihood = -745.20057
Iteration 3: log likelihood = -744.79325
Iteration 4: log likelihood = -744.79049
Iteration 5: log likelihood = -744.79049
```

Log-normal regression --

```
accelerated failure-time form      Number of obs      =      30726
Inverse-Gaussian shared frailty    Number of groups   =      116
Group variable: discode
```

```
No. of subjects =      653      Obs per group: min =      1
No. of failures =      392      avg = 264.8793
Time at risk    = 30392.64662    max =      6100
```

```
Log likelihood = -744.79049      LR chi2(2)         =      51.71
Prob > chi2     =      0.0000
```

_t	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
dynstafc	-.0009535	.0003636	-2.62	0.009	-.0016662 - .0002408
dyn_pdufadum	-.2074658	.2016818	-1.03	0.304	-.6027548 .1878233
_cons	4.349167	.4298839	10.12	0.000	3.50661 5.191724

/ln_sig		-.1795281	.0629746	-2.85	0.004	-.3029559	-.0561002
/ln_the		-.1279533	.3038382	-0.42	0.674	-.7234653	.4675586

sigma		.8356645	.0526256			.7386316	.9454444
theta		.8798944	.2673455			.4850685	1.596093

Likelihood-ratio test of theta=0: chibar2(01) = 145.30 Prob>=chibar2 = 0.000

```
. streg dynstafc dyn_pdufadum orderent wpnoavg3, dist(lognormal) frailty(invgaussian) shared(discodes)
> ssian) shared(discodes)
```

```
failure _d: aprovdum
analysis time _t: acttime
id: drugnum
```

Fitting comparison lnnormal model:

Fitting constant-only model:

```
Iteration 0: log likelihood = -728.22812 (not concave)
Iteration 1: log likelihood = -676.06314
Iteration 2: log likelihood = -667.7861
Iteration 3: log likelihood = -667.71774
Iteration 4: log likelihood = -667.7177
```

Fitting full model:

```
Iteration 0: log likelihood = -675.38109
Iteration 1: log likelihood = -649.74824
Iteration 2: log likelihood = -648.48064
Iteration 3: log likelihood = -648.47878
Iteration 4: log likelihood = -648.47878
```

Log-normal regression --

```
accelerated failure-time form          Number of obs    = 25229
Inverse-Gaussian shared frailty       Number of groups  = 109
Group variable: discodes
```

```
No. of subjects = 527          Obs per group: min = 1
No. of failures = 344         avg = 231.4587
Time at risk    = 24960.52604 max = 5662
```

```
LR chi2(4) = 38.48
Log likelihood = -648.47878 Prob > chi2 = 0.0000
```

_t		Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
dynstafc		-.0009768	.0003932	-2.48	0.013	-.0017475 - .0002061
dyn_pdufadum		-.1564736	.2124759	-0.74	0.461	-.5729187 .2599715
orderent		-.0016992	.0071881	-0.24	0.813	-.0157876 .0123892
wpnoavg3		.0002542	.0003845	0.66	0.509	-.0004994 .0010078
_cons		4.349706	.4661625	9.33	0.000	3.436044 5.263367

/ln_sig		-.138926	.0672558	-2.07	0.039	-.270745 - .0071071
/ln_the		-.2448122	.3234753	-0.76	0.449	-.8788121 .3891877

sigma		.8702924	.0585322			.762811 .9929181
theta		.7828515	.2532331			.4152759 1.475782

Likelihood-ratio test of theta=0: chibar2(01) = 94.21 Prob>=chibar2 = 0.000

```
. streg dynstafc dyn_pdufadum orderent fsubmits, dist(lognormal) frailty(invgaus
> ssian) shared(discode)
```

```
failure _d: aprovdum
analysis time _t: acttime
id: drugnum
```

Fitting comparison lnnormal model:

Fitting constant-only model:

```
Iteration 0: log likelihood = -618.93602 (not concave)
Iteration 1: log likelihood = -544.49342
Iteration 2: log likelihood = -532.1574
Iteration 3: log likelihood = -527.15535
Iteration 4: log likelihood = -527.15028
Iteration 5: log likelihood = -527.15028
```

Fitting full model:

```
Iteration 0: log likelihood = -496.75855
Iteration 1: log likelihood = -485.32222
Iteration 2: log likelihood = -484.89206
Iteration 3: log likelihood = -484.89056
Iteration 4: log likelihood = -484.89056
```

Log-normal regression --

```
accelerated failure-time form      Number of obs      =      12950
Inverse-Gaussian shared frailty    Number of groups   =       115
Group variable: discode
```

```
No. of subjects =          438      Obs per group: min =          1
No. of failures =          366      avg =      112.6087
Time at risk    =      12730.2904    max =          1946
```

```
Log likelihood = -484.89056      LR chi2(4)          =          84.52
Prob > chi2      =          0.0000
```

_t	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
dynstafc	-.0008315	.0003247	-2.56	0.010	-.001468	-.000195
dyn_pdufadum	-.256765	.174583	-1.47	0.141	-.5989413	.0854113
orderent	.0156398	.0050304	3.11	0.002	.0057804	.0254991
fsubmits	-.0263828	.007139	-3.70	0.000	-.0403748	-.0123907
_cons	4.340696	.3748293	11.58	0.000	3.606044	5.075348
/ln_sig	-.2692082	.0475812	-5.66	0.000	-.3624656	-.1759507
/ln_the	-1.169103	.3815181	-3.06	0.002	-1.916865	-.4213414
sigma	.7639842	.0363513			.6959582	.8386593
theta	.3106454	.1185169			.1470673	.6561661

Likelihood-ratio test of theta=0: chibar2(01) = 24.24 Prob>=chibar2 = 0.000

```
. streg dynstafc dyn_pdufadum orderent, dist(lognormal) frailty(invgaussian) sh
> ared(discode)
```

```
failure _d: aprovdum
analysis time _t: acttime
id: drugnum
```


Fitting comparison lnnormal model:

Fitting constant-only model:

Iteration 0: log likelihood = -786.84798 (not concave)
Iteration 1: log likelihood = -717.93862
Iteration 2: log likelihood = -714.29652
Iteration 3: log likelihood = -714.28935
Iteration 4: log likelihood = -714.28935

Fitting full model:

Iteration 0: log likelihood = -722.25529
Iteration 1: log likelihood = -694.81175
Iteration 2: log likelihood = -692.42105
Iteration 3: log likelihood = -692.41501
Iteration 4: log likelihood = -692.41501

Log-normal regression --

accelerated failure-time form
Inverse-Gaussian shared frailty

Number of obs = 27236
Number of groups = 116

Group variable: discode

No. of subjects = 584
No. of failures = 376
Time at risk = 26936.25207
Obs per group: min = 1
 avg = 234.7931
 max = 6100

Log likelihood = -692.41501
LR chi2(3) = 43.75
Prob > chi2 = 0.0000

_t	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
dynstafc	-.0008316	.0003688	-2.26	0.024	-.0015543	-.0001088
dyn_pdufadum	-.2214869	.2031671	-1.09	0.276	-.6196871	.1767133
orderent	-.00203	.0067132	-0.30	0.762	-.0151877	.0111276
_cons	4.209489	.4345071	9.69	0.000	3.35787	5.061107
/ln_sig	-.1851673	.0631846	-2.93	0.003	-.3090068	-.0613279
/ln_the	-.2296099	.3080288	-0.75	0.456	-.8333353	.3741154
sigma	.8309652	.0525042			.7341758	.9405148
theta	.7948436	.2448347			.4345974	1.453705

Likelihood-ratio test of theta=0: chibar2(01) = 104.52 Prob>=chibar2 = 0.000

Estimates with Firm Fixed Effects

```
. streg dynstafc dyn_pdufadum orderent fmx*, dist(lognormal) frailty(invgaussia
> n) shared(discode)
```

```
      failure _d:  aprovdum
      analysis time _t:  acttime
                   id:  drugnum
note: fmxAkzoNobel dropped due to collinearity
note: fmxBiogen dropped due to collinearity
note: fmxNovoNordisk dropped due to collinearity
note: fmxPierreFabre dropped due to collinearity
note: fmxSankyo dropped due to collinearity
note: fmxTEVA dropped due to collinearity
note: fmxUCB dropped due to collinearity
```

Fitting comparison lnnormal model:

Fitting constant-only model:

```
Iteration 0:  log likelihood = -786.84798  (not concave)
Iteration 1:  log likelihood = -717.93862
Iteration 2:  log likelihood = -714.29652
Iteration 3:  log likelihood = -714.28935
Iteration 4:  log likelihood = -714.28935
```

Fitting full model:

```
Iteration 0:  log likelihood = -658.23975
Iteration 1:  log likelihood = -629.70568
Iteration 2:  log likelihood = -628.84433
Iteration 3:  log likelihood = -628.83567
Iteration 4:  log likelihood = -628.83567
```

Log-normal regression --

```
      accelerated failure-time form      Number of obs      =      27236
      Inverse-Gaussian shared frailty    Number of groups    =      116
Group variable:  discode
```

```
No. of subjects =      584      Obs per group: min =      1
No. of failures =      376      avg = 234.7931
Time at risk    = 26936.25207    max =      6100
```

```
Log likelihood = -628.83567      LR chi2(53)      =      170.91
                                Prob > chi2      =      0.0000
```

	_t	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
dynstafc		-0.0006635	.0003639	-1.82	0.068	-0.0013768 .0000497
dyn_pdufadum		-.3219667	.199172	-1.62	0.106	-.7123366 .0684032
orderent		.0067275	.0063239	1.06	0.287	-.0056671 .0191221
fmx3M		-1.418105	.7607534	-1.86	0.062	-2.909154 .0729444
fmxAbbott		-1.119761	.3122634	-3.59	0.000	-1.731786 -.5077354
fmxAlcon		-.9960038	.3904991	-2.55	0.011	-1.761368 -.2306397
fmxAllergan		-.6880035	.4712937	-1.46	0.144	-1.611722 .2357151
fmxAmHomeP~s		.9000141	1.25873	0.72	0.475	-1.567052 3.36708
fmxAmgen		3.237313	784.3181	0.00	0.997	-1533.998 1540.473
fmxAstaMed~a		-2.050024	.9052912	-2.26	0.024	-3.824362 -.2756862
fmxAstra		-1.18924	.6884696	-1.73	0.084	-2.538616 .1601351
fmxAventis		-.0628254	.6733378	-0.09	0.926	-1.382543 1.256893
fmxBayer		-1.215244	.3228096	-3.76	0.000	-1.84794 -.5825492

fmxBoehringer	-.9321594	.3851426	-2.42	0.016	-1.687025	-.1772937
fmxBMS	-.9840444	.2489887	-3.95	0.000	-1.472053	-.4960356
fmxCibaGeigy	-.8607293	.3357076	-2.56	0.010	-1.518704	-.2027544
fmxDuPont	-1.092569	1.141616	-0.96	0.339	-3.330095	1.144957
fmxEliLilly	-1.068409	.3168909	-3.37	0.001	-1.689503	-.4473139
fmxFujisawa	-.8837002	.5159016	-1.71	0.087	-1.894849	.1274484
fmxGenentech	2.302135	2023.759	0.00	0.999	-3964.193	3968.797
fmxGenzyme	-.6484862	.9074282	-0.71	0.475	-2.427013	1.13004
fmxGlaxo	-1.163541	.437423	-2.66	0.008	-2.020874	-.3062072
fmxGlaxoWeise	-.8324015	.2646015	-3.15	0.002	-1.351011	-.3137922
fmxHoechst	-.8305172	.3416838	-2.43	0.015	-1.500205	-.1608291
fmxJohnson&Johnson	-.5229147	.2584165	-2.02	0.043	-1.029402	-.0164276
fmxMallinckrodt	-.4558742	.7372733	-0.62	0.536	-1.900903	.989155
fmxMerck	-1.344296	.2297476	-5.85	0.000	-1.794593	-.8939987
fmxSearle	-1.679922	.9740835	-1.72	0.085	-3.589091	.2292468
fmxMylan	-1.052396	.9187704	-1.15	0.252	-2.853153	.7483607
fmxNovartis	-.4597173	.6598407	-0.70	0.486	-1.752981	.8335468
fmxOno	3.64905	584.6371	0.01	0.995	-1142.219	1149.517
fmxOrganon	-.4599829	.6581291	-0.70	0.485	-1.749892	.8299263
fmxOtsuka	.2648683	.674279	0.39	0.694	-1.056694	1.586431
fmxPfizer	-.7061153	.2579201	-2.74	0.006	-1.21163	-.2006011
fmxPharmacia	-.6589514	.2823826	-2.33	0.020	-1.212411	-.1054916
fmxProcter&Kingsley	.0502309	.6576201	0.08	0.939	-1.238681	1.339143
fmxRhone	-.7202654	.4590784	-1.57	0.117	-1.620043	.1795118
fmxRoche	-.9345687	.2272238	-4.11	0.000	-1.379919	-.4892183
fmxSandoz	-.8755954	.4460083	-1.96	0.050	-1.749756	-.0014352
fmxSanofi	-1.113875	.4788177	-2.33	0.020	-2.052341	-.1754098
fmxSchering	-1.352224	.5100118	-2.65	0.008	-2.351829	-.3526195
fmxSchering-Plough	.0158493	.4232806	0.04	0.970	-.8137654	.8454641
fmxSearle2	-.1699128	.5617709	-0.30	0.762	-1.270964	.9311379
fmxSKB	-1.202241	.3064334	-3.92	0.000	-1.802839	-.6016423
fmxSolvay	.4790672	.8539772	0.56	0.575	-1.194697	2.152832
fmxSyntex	-.78377	.3759198	-2.08	0.037	-1.520559	-.0469807
fmxTakeda	.006862	.8193108	0.01	0.993	-1.598958	1.612682
fmxUpjohn	-.6968433	.4518556	-1.54	0.123	-1.582464	.1887774
fmxWarnerLambert	-1.090645	.3871473	-2.82	0.005	-1.84944	-.3318506
fmxBurroughs	-1.321466	.303295	-4.36	0.000	-1.915914	-.7270191
fmxWyethAyerst	-.5018613	.3093156	-1.62	0.105	-1.108109	.1043862
fmxZambon	.1163114	.9090226	0.13	0.898	-1.66534	1.897963
fmxZeneca	-.8699431	.4141982	-2.10	0.036	-1.681757	-.0581296
_cons	4.6031	.4341062	10.60	0.000	3.752267	5.453932

/ln_sig	-.2342478	.0627818	-3.73	0.000	-.3572979	-.1111978
/ln_the	-.5058134	.3413921	-1.48	0.138	-1.17493	.1633029

sigma	.7911657	.0496708			.6995641	.8947618
theta	.6030149	.2058645			.3088407	1.177393

Likelihood-ratio test of theta=0: chibar2(01) = 55.46 Prob>=chibar2 = 0.000

Gompertz Estimates

NOTE THAT STATA REPORTS GOMPERTZ MODEL COEFFICIENTS IN TERMS OF HAZARD RATIOS. HENCE A HAZARD RATIO GREATER THAN ONE REPRESENTS AN INCREASED EFFECT UPON THE HAZARD, CORRESPONDING TO A DECREASE IN THE APPROVAL TIME.

```
. streg dynstafc dyn_pdufadum orderent, dist(gompertz) frailty(invgaussian) sha
> red(discodes)
```

```
failure _d: aprovdum
analysis time _t: acttime
id: drugnum
```

Fitting comparison gompertz model:

Fitting constant-only model:

```
Iteration 0: log likelihood = -808.81266 (not concave)
Iteration 1: log likelihood = -771.16012
Iteration 2: log likelihood = -755.43241
Iteration 3: log likelihood = -755.26649
Iteration 4: log likelihood = -755.2664
Iteration 5: log likelihood = -755.2664
```

Fitting full model:

```
Iteration 0: log likelihood = -756.07974
Iteration 1: log likelihood = -742.89346
Iteration 2: log likelihood = -740.50727
Iteration 3: log likelihood = -740.35113
Iteration 4: log likelihood = -740.34224
Iteration 5: log likelihood = -740.3415
Iteration 6: log likelihood = -740.34144
```

Gompertz regression --

```
log relative-hazard form          Number of obs    =    27236
Inverse-Gaussian shared frailty   Number of groups  =     116
```

Group variable: discodes

```
No. of subjects =          584          Obs per group: min =          1
No. of failures =          376                      avg =   234.7931
Time at risk    =   26936.25207                    max =          6100
```

```
Log likelihood =   -740.34144          LR chi2(3)        =          29.85
                                          Prob > chi2      =          0.0000
```

	_t	Haz. Ratio	Std. Err.	z	P> z	[95% Conf. Interval]	
dynstafc		1.000861	.0004276	2.01	0.044	1.000023	1.001699
dyn_pdufadum		1.279959	.2904187	1.09	0.277	.8204667	1.996784
orderent		.9857137	.0087936	-1.61	0.107	.9686284	1.0031
gamma		-.0136558	.0016975	-8.04	0.000	-.0169828	-.0103289
/ln_the		-1.438888	.3624099	-3.97	0.000	-2.149198	-.7285775
theta		.2371914	.0859605			.1165776	.482595

Likelihood-ratio test of theta=0: chibar2(01) = 28.86 Prob>=chibar2 = 0.000

Marginal Effects from the Gompertz Model with Time-Varying Covariates.

NOTE THAT FOR MARGINAL EFFECTS ARE CALCULATED IN TERMS OF MARGINAL EFFECT UPON THE EXPECTED APPROVAL TIME. SO A NEGATIVE ESTIMATE IMPLIES THAT AN INCREASE IN CDER STAFF IS ASSOCIATED WITH A DECREASE IN EXPECTED APPROVAL TIME.

```
. mfx compute, dydx
```

```
Marginal effects after gompertzhet  
y = predicted median _t (predict)  
= 26.310384
```

```
-----  
variable |      dy/dx   Std. Err.    z    P>|z|   [      95% C.I.      ]      X  
-----+-----  
dynstafc |  -.0272491   .01467   -1.86   0.063  -.055999   .001501   1343.66  
dyn_pd~m*| -7.597384   7.03124   -1.08   0.280  -21.3784   6.18359   .401234  
orderent |  .4555331   .33741    1.35   0.177  -.205779   1.11685   12.504  
-----
```

(*) dy/dx is for discrete change of dummy variable from 0 to 1

```
. log close  
log: C:\fdatemp\dyn-stafcder-run20040127.log  
log type: text  
closed on: 28 Jan 2004, 01:18:20  
-----
```