This note lists some statistical estimates on which the analysis and discussion in the Health Affairs article was based.

All models were estimated in **STATA 8.0**. As a check, I am currently developing several estimators for this problem (and related ones) in **R**. These include models in which NDA submissions are endogenous to regulatory action, and models in which there are competing risks. Check back in a few months and I’ll try to post those runs on the website by then.

**Methodological Points: Robustness to Alternative Distributional Assumptions and Inclusion of Firm- and Disease- Indicator Variables**

I begin with “full-sample” models which include (1) fixed effects for the firm submitting the NDA and (2) shared frailties (essentially a form of “random effects” in duration models) for the primary indication of the NDA. This essentially controls for all disease-level and firm-level factors associated with approval times. I present these under eight different distributional assumptions.

- Weibull, gamma frailty
- Weibull, inverse Gaussian frailty
- Lognormal, gamma frailty
- Lognormal, inverse Gaussian frailty
- Gamma, gamma frailty
- Log-logistic, gamma frailty
- Gompertz, gamma frailty
- Cox model with firm fixed-effects only

**Confounding Influences.** It is worth repeating what we acknowledge explicitly in the article: that our analysis is observational, not experimental. Put differently, the effect of staff cannot be experimentally differentiated from other changes occurring at the same time. While no model can fully account for

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1 I generate fixed effects for firms and shared frailties (akin to random effects) for primary indications because this is the easiest way to facilitate estimation of the maximum likelihood models here that allows for convergence without non-concavity in the iterations of the likelihood maximization.
these effects, all of our models do include a “time trend,” in the form of the year of submission of the NME, which at least rules out those mechanisms that increased/decreased linearly with time (we can also include quadratic and cubic functions of time, neither of which change the results here appreciably). In addition, in other models (not reported here but which we can send you if necessary) we have controlled for changes in presidential administration, congressional committee oversight, and other political variables that may capture some of the politically influenced changes in FDA procedure that were occurring during the period in which our sample was generated.

I then report estimates from a number of models in which a number of observed covariates are added to estimation. These include both epidemiological and firm-level covariates.

Outliers/Influential Observations. Finally I do one check on influential observations in one of the simplest models, namely excluding the top percentile of observations (which in a duration model context are subject to being outliers) and re-estimating the likelihood equation. The last two pages of the notes show that this sample exclusion makes little difference to the results. Obviously other tests could be run here, but for a first glance this shows that influential positive outliers are not an issue.

Competing Risks. I have not presented competing risks models here but I can pass along estimations that show that a competing risks framework does not change the substantive findings.

Format of Presentation. In what follows I will present a number of model runs by printing the relevant output from STATA8. I have in most cases suppressed the printing of log-likelihood values at successive iterations of maximum likelihood convergence, as well as coefficient values for firm-level fixed effects and primary-indication-level random effects (combined, there are nearly 250 of these in the models with the largest samples).

One final note on presentation. I have marked marginal effects estimates for the CDER staff variable (STAFCDER) in **aqua blue**. Notes about the interpretation of coefficients and effects/elasticities appear in **yellow**.
Weibull model, Gamma Frailty, Complete Battery of Fixed Effects for Firms and Shared Frailties for Primary Indications, and control for Time Trend.

NOTICE THAT THE COEFFICIENTS ARE IN HAZARD FORM, SO POSITIVE COEFFICIENT MEANS INCREASE IN APPROVAL PROBABILITY AND REDUCTION IN APPROVAL TIME.

```
streg stafcder subyear fmx*, dist(weibull) frailty(gamma) shared(discord)
```

```
|                      |     _t | Haz. Ratio | Std. Err. |      z | P>|z| |  [95% Conf. Interval] |
|----------------------|--------|------------|-----------|-------|-----|----------------------|
| stafcder             | 1.002479 | .0005501   | 4.51      | 0.000 | 1.001402 | 1.003558 |
| subyear              | 1.020743 | .0234056   | 0.90      | 0.371 | .975884 | 1.067663 |
| /ln_p                | .4515741 | .0302051   | 14.95     | 0.000 | .3923732 | .5107751 |
| /ln_the              | -.8854326 | .22576    | -3.92     | 0.000 | -1.327914 | -.4429512 |
| p                    | 1.570783 | .0474457   |           |    | 1.48049 | 1.666583 |
| 1/p                  | .6366252 | .0192294   |           |    | .6000303 | .675452 |
| theta                | .4125357 | .093134    |           |    | .2650295 | .6421385 |
```

Likelihood-ratio test of theta=0: chibar2(01) = 71.56 Prob > chibar2 = 0.000

NOTICE THAT MARGINAL EFFECTS AND ELASTICITIES FOR WEIBULL MODEL ARE REPORTED IN TERMS OF PREDICTED MEDIAN APPROVAL TIME, SO A NEGATIVE COEFFICIENT MEANS A REDUCTION IN REVIEW TIME.

```
mfx compute, dydx
```

Marginal effects after weibullhet

```
| variable | dy/dx | Std. Err. |      z | P>|z| |  [95% C.I. ] | X  |
|----------|-------|-----------|-------|-----|----------------|----|
| stafcder | -.0543998 | .01161   | -4.69 | 0.000 | -.077149 | -.031651 | 1299.47 |
| subyear  | .1976721  | .43943   | 0.45  | 0.653 | -.663593 | 1.05894  | 1988.95 |
| orderent | .3253007  | .22441   | 1.45  | 0.147 | -.114529 | .76513   | 8.83312 |
```

```
mfx compute, eyex
```

Elasticities after weibullhet

```
| variable | ey/ex | Std. Err. |      z | P>|z| |  [95% C.I. ] | X  |
|----------|-------|-----------|-------|-----|----------------|----|
| stafcder | -.2.701623 | .51826   | -5.21 | 0.000 | -3.7174 | -1.68585 | 1299.47 |
| subyear  | 15.02563 | 33.529   | 0.45  | 0.654 | -50.6892 | 80.7404  | 1988.95 |
| orderent | .109815  | .07024   | 1.56  | 0.118 | -.027847 | .247477  | 8.83312 |
```
Weibull model, Inverse Gaussian Frailty, Complete Battery of Fixed Effects for Firms and Shared Frailties for Primary Indications, and Control for Time Trend.

NOTICE THAT THE COEFFICIENTS ARE IN HAZARD FORM, SO POSITIVE COEFFICIENT MEANS INCREASE IN APPROVAL PROBABILITY AND REDUCTION IN APPROVAL TIME.

. streg stafcder subyear fmx*, dist(weibull) frailty(invg) shared(discode)

note: fmxAkzoNobel dropped due to collinearity
note: fmxBiogen dropped due to collinearity
note: fmxPierreFabre dropped due to collinearity

Weibull regression --
                  log-relative hazard form                     Number of obs      =       843
                  Inverse-Gaussian shared frailty        Number of groups   =       180
Group variable: discode
No. of subjects =          843                  Obs per group: min =         1
No. of failures =          523                                 avg =  4.683333
Time at risk    =  36292.47129                                 max =        85
Log likelihood  =   -841.98304                  LR chi2(56)        =    435.60
                  Prob > chi2        =    0.0000
------------------------------------------------------------------------------
   _t | Haz. Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
   stafcder |   1.002464   .0005545     4.45   0.000     1.001378    1.003552
   subyear |   1.022313   .0235693     0.96   0.338     .9771458    1.069567
                  /ln_p |    .453745   .0302342    15.01   0.000      .394487    .5130029
                  /ln_the |  -.4148135   .3140935    -1.32   0.187    -1.030426    .2007985
-------------+----------------------------------------------------------------
              p |   1.574196   .0475946                      1.483623    1.670299
             1/p |   .6352447   .0192061                      .5986951    .6740257
              theta |   .6604634   .2074473                      .3568551    1.222378
------------------------------------------------------------------------------
Likelihood-ratio test of theta=0: chibar2(01) =    70.54 Prob>=chibar2 = 0.000

NOTICE THAT MARGINAL EFFECTS AND ELASTICITIES FOR WEIBULL MODEL ARE REPORTED IN TERMS OF PREDICTED MEDIAN APPROVAL TIME, SO A NEGATIVE COEFFICIENT MEANS A REDUCTION IN REVIEW TIME.

. mfx compute, dydx
Marginal effects after weibullhet
y  = predicted median _t (predict) =  25.056163

variable |      dy/dx    Std. Err.     z    P>|z|  [    95% C.I.   ]      X
---------+--------------------------------------------------------------------
 stafcder |  -.0595963      .01145   -5.21   0.000  -.082036 -.037157   1296.46
 subyear |   .4540731      .41845    1.09   0.278  -.366078  1.27422   1988.93
---------+--------------------------------------------------------------------

. mfx compute, eyex
Elasticities after weibullhet
y  = predicted median _t (predict) =  25.056163

variable |      ey/ex    Std. Err.     z    P>|z|  [    95% C.I.   ]      X
---------+--------------------------------------------------------------------
 stafcder |  -3.083643      .52139   -5.91   0.000  -.4.10554 -2.06174  1296.46
 subyear |   36.04379      33.107    1.09   0.276  -28.8444  100.932   1988.93
---------+--------------------------------------------------------------------
Lognormal Model, Gamma Frailty, Complete Battery of Fixed Effects for Firms and Shared Frailties for Primary Indication, with control for time trend

NOTICE THAT COEFFICIENTS, MARGINAL EFFECTS AND ELASTICITIES FOR LOGNORMAL MODEL ARE REPORTED IN TERMS OF PREDICTED MEDIAN APPROVAL TIME, SO A NEGATIVE COEFFICIENT MEANS A REDUCTION IN REVIEW TIME.

. streg stafcder subyear fm**, dist(logn) frailty(gamma) shared(discode)
note: fmxAkzoNobel dropped due to collinearity
note: fmxBiogen dropped due to collinearity
note: fmxPierreFabre dropped due to collinearity

Log-normal regression -- 
Accelerated failure-time form  Number of obs = 843
Gamma shared frailty  Number of groups = 180
Group variable: discode

|                | Coef.   | Std. Err. | z    | P>|z|  | [95% Conf. Interval] |
|----------------|---------|-----------|------|------|----------------------|
| stafcder       | -.0013  | .00035   | -3.64| 0.000| -.0020109 -.0006021 |
| subyear        | -.0109  | .01505   | -0.73| 0.465| -.0405028 .0185051  |
| _cons          | 27.2131 | 29.5131  |     |      |                      |

|                | Coef.   | Std. Err. | z    | P>|z|  | [95% Conf. Interval] |
|----------------|---------|-----------|------|------|----------------------|
| /ln_sig        | -.3177  | .0447    | -7.11| 0.000| -.4053662 -.2301171 |
| /ln_the        | -1.0613| .2226    | -4.77| 0.000| -1.497584 -0.6250432|

|                | Coef.   | Std. Err. | z    | P>|z|  | [95% Conf. Interval] |
|----------------|---------|-----------|------|------|----------------------|
| sigma          | .7278   | .0325    | 23.13| 0.000| .6667326 .7944406   |
| theta          | .3460   | .0770    | 4.48| 0.000| .22367 .5352383    |

Likelihood-ratio test of theta=0: chibar2(01) = 82.56 Prob>|chibar2| = 0.000

. mfx compute, dydx
Marginal effects after lnormalhet
y = predicted median _t (predict) = 22.181383

|                | dy/dx   | Std. Err. | z    | P>|z|  | [95% C.I. ] |
|----------------|---------|-----------|------|------|-----------|
| stafcder       | -.0242  | .0083     | -2.90| 0.004| -.040493  -.007858 |
| subyear        | -.3751  | .3427     | -1.09| 0.274| -1.04682  .296553 |

. mfx compute, eyex
Elasticities after lnormalhet
y = predicted median _t (predict) = 22.181383

|                | ey/ex   | Std. Err. | z    | P>|z|  | [95% C.I. ] |
|----------------|---------|-----------|------|------|-----------|
| stafcder       | -1.41   | .4725     | -2.99| 0.003| -2.33899  -.487027 |
| subyear        | -33.64  | 30.65     | -1.10| 0.273| -93.7186  26.4446 |

---
LogNormal Model, Inverse Gaussian frailty, full battery of fixed effects for firms and Shared Frailties for diseases, with control for time trend.

NOTICE THAT COEFFICIENTS, MARGINAL EFFECTS AND ELASTICITIES FOR LOGNORMAL MODEL ARE REPORTED IN TERMS OF PREDICTED MEDIAN APPROVAL TIME, SO A NEGATIVE COEFFICIENT MEANS A REDUCTION IN REVIEW TIME.

```
. streg stafcder subyear fmx*, dist(logn) frailty(invg) shared(discode)
note: fmxAkzoNobel dropped due to collinearity
note: fmxBiogen dropped due to collinearity
note: fmxPierreFabre dropped due to collinearity

Log-normal regression -- accelerated failure-time form
Inverse-Gaussian shared frailty
Number of obs = 843
Group variable: discode
Number of groups = 180
Group variable: discode
No. of subjects = 843
Obs per group: min = 1
No. of failures = 523
avg = 4.683333
Time at risk = 36292.47129
max = 85
Log likelihood = -833.69242
LR chi2(56) = 265.81
Prob > chi2 = 0.0000

------------------------------------------------------------------------------
    _t |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
   stafcder |  -.0013295   .0003609    -3.68   0.000     -.002037   -.0006221
   subyear |   -.01015   .0151241    -0.67   0.502    -.0397927    .0194927
     _cons |   25.56375   29.65355     0.86   0.389    -32.55614    83.68365
------------------------------------------------------------------------------
     /ln_sig |   -.319232     .04715    -6.77   0.000    -.4116443   -.2268196
     /ln_the |  -.7299569   .2840916    -2.57   0.010    -.1286766   -.1731476
------------------------------------------------------------------------------
sigma |   .726707   .0342643                      .6625599    .7970646
theta |   .4819298   .1369122                      .2761624    .8410135
------------------------------------------------------------------------------
Likelihood-ratio test of theta=0: chi2(01) = 80.29 Prob>chi2 = 0.0000

. mfx compute, dydx
Marginal effects after lnormalhet
y  = predicted median _t (predict)
    = 21.931525

variable |      dy/dx    Std. Err.     z    P>|z|  [ 95% C.I. ]      X
---------+--------------------------------------------------------------------
   stafcder |  -.025024      .00833   -3.00   0.003  -.041358  -.00869   1296.46
   subyear |  -.3357476      .34125   -0.98   0.325  -1.00459  .333092   1988.93
---------+--------------------------------------------------------------------

. mfx compute, eyex
Elasticities after lnormalhet
y  = predicted median _t (predict)
    = 21.931525

variable |      ey/ex    Std. Err.     z    P>|z|  [ 95% C.I. ]      X
---------+--------------------------------------------------------------------
   stafcder |  -1.479271      .47629   -3.11   0.002  -2.41279  -.54575    1296.46
   subyear |  -30.44832      30.839   -0.99   0.323   -90.8915   29.9948    1988.93
---------+--------------------------------------------------------------------
```
Gompertz Model, Gamma Frailty, Complete Battery of Fixed Effects for Firms and Random Effects for Primary Indication, with control for time trend

**NOTICE THAT THE COEFFICIENTS ARE IN HAZARD FORM, SO POSITIVE COEFFICIENT MEANS INCREASE IN APPROVAL PROBABILITY AND REDUCTION IN APPROVAL TIME.**

```
. streg stafcder subyear fm*, dist(gomp) frailty(gamma) shared(discode)
```

**NOTICE THAT THE COEFFICIENTS ARE IN HAZARD FORM, SO POSITIVE COEFFICIENT MEANS INCREASE IN APPROVAL PROBABILITY AND REDUCTION IN APPROVAL TIME.**

```
mfx compute, dydx
```

```
mfx compute, eyex
```

| stafcder | -.0485965 | .01348 | -3.60 | 0.000 | -.07502 | -.022173 | 1296.46 |
| subyear  | .2385155  | .52045 | 0.46  | 0.647 | -.781554 | 1.25859  | 1988.93 |

**NOTICE THAT MARGINAL EFFECTS AND ELASTICITIES FOR GOMPERTZ MODEL ARE REPORTED IN TERMS OF PREDICTED MEDIAN APPROVAL TIME, SO A NEGATIVE COEFFICIENT MEANS A REDUCTION IN REVIEW TIME.**
Gamma model, Gamma frailty, with control for time trend. (Gamma model does not support shared frailties in STATA8, so frailty is not grouped here.)

NOTICE THAT COEFFICIENTS, MARGINAL EFFECTS AND ELASTICITIES FOR LOGNORMAL MODEL ARE REPORTED IN TERMS OF PREDICTED MEDIAN APPROVAL TIME, SO A NEGATIVE COEFFICIENT MEANS A REDUCTION IN REVIEW TIME.

```
.streg stafcder subyear, dist(gamma) frailty(gamma)
```

Gamma regression -- accelerated failure-time form

|                | Coef.       | Std. Err. | z    | P>|z| | [95% Conf. Interval] |
|----------------|-------------|-----------|------|-----|----------------------|
| _t             |             |           |      |     |                      |
| stafcder       | -.0010883   | .0003272  | -3.33| 0.001| -.0017295             | -.0004471             |
| subyear        | -.0266162   | .0136876  | -1.94| 0.052| -.0534435             | .0002111              |
| _cons          | 57.4792     | 26.83101  | 2.14 | 0.032| 4.891391              | 110.067               |
| /ln_sig        | -.7833145   | .0886469  | -8.84| 0.000| -.9570591             | -.6095698             |
| /kappa         | .5874128    | .1080451  | 5.44 | 0.000| .3756482              | .7991774              |
| /ln_the        | .8615113    | .1492063  | 5.77 | 0.000| .5690724              | 1.15395               |
| sigma          | .4568891    | .0405018  | 11.06| 0.000| .3840206              | .5435846              |
| theta          | 2.366735    | .3531317  | 6.69 | 0.000| 1.766627              | 3.170693              |

Likelihood-ratio test of theta=0: chibar2(01) = 73.01 Prob > chibar2 = 0.000

```
.mfx compute, dydx
```

Marginal effects after gammahet

```
variable | dy/dx    Std. Err.    z   P>|z|   [ 95% C.I.  ]   X
---------|----------|-----------------|-------|-----|-------------------|
stafcder | -.0343231| .0105           | -3.27 | 0.001| -.0549 to -.013746| 1296.46           |
subyear  | -.8394486| .43222          | -1.94 | 0.052| -1.68658 to .007679| 1988.93           |

```

```
.mfx compute, eyex
```

Elasticities after gammahet

```
variable | ey/ex    Std. Err.    z   P>|z|   [ 95% C.I.  ]   X
---------|----------|-----------------|-------|-----|-------------------|
stafcder | -1.410907| .42414          | -3.33 | 0.001| -2.24221 to -.579607| 1296.46           |
subyear  | -52.9378 | 27.224          | -1.94 | 0.052| -106.295 to .4197777| 1988.93           |
```
Log-Logistic Model, Gamma Frailty, with Full Battery of Fixed and Random Effects for Firms and Diseases, with Control for Time Trend

NOTICE THAT COEFFICIENTS, MARGINAL EFFECTS AND ELASTICITIES FOR LOGLOGISTIC MODEL ARE REPORTED IN TERMS OF PREDICTED MEDIAN APPROVAL TIME, SO A NEGATIVE COEFFICIENT MEANS A REDUCTION IN REVIEW TIME.

.streg stafcder subyear fmx*, dist(loglog) frailty(gamma) shared(discode)

note: fmxAkzoNobel dropped due to collinearity
note: fmxBiogen dropped due to collinearity
note: fmxPierreFabre dropped due to collinearity

Log-logistic regression --
accelerated failure-time form
Gamma shared frailty

Number of obs  =  843
Gamma shared frailty
Number of groups  =  180
Group variable: discode

No. of subjects  =  843
Obs per group: min  =  1
No. of failures  =  523
avg  =  4.683333
Time at risk  =  36292.47129
max  =  85

Log likelihood  =  -816.12435
LR chi2(56)  =  251.28
Prob > chi2  =  0.0000

------------------------------------------------------------------------------
  _t |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  stafcder |  -.001028   .0003329    -3.09   0.002    -.0016805   -.0003754
  subyear |  -.0156374   .0140761    -1.11   0.267    -.0432261    .0119514
  _cons  |   35.85387   27.60132     1.30   0.194    -18.24372    89.95146
-------------+----------------------------------------------------------------
 /ln_gam  |  -1.024648   .0569088   -18.01   0.000    -1.136187   -.9131087
 /ln_the  |  -.7705357   .1954608    -3.94   0.000    -1.153632   -.3874396
-------------+----------------------------------------------------------------
  gamma  |   .3589228   .0204259                      .3210408    .4012748
  theta  |   .4627651   .0904524                      .3154889    .6787926
------------------------------------------------------------------------------

Likelihood-ratio test of theta=0: chibar2(01) =  114.60 Prob>chibar2 =  0.0000

.mfx compute, dydx
Marginal effects after llogistic
  y  = predicted median _t (predict)
     =  20.063503

|          | dy/dx    | Std. Err. |     z  | P>|z|      | [95% C.I. ] |      X         |
|----------|----------|-----------|-------|---------|------------|-------------|
| stafcder | -.0160747| .00644    | -2.49 | 0.013   | -.028704   | -.003445    | 1296.46     |
| subyear  | -.507045 | .27307    | -1.86 | 0.063   | -1.04224   | .028155     | 1988.93     |

.mfx compute, eyex
Elasticities after llogistic
  y  = predicted median _t (predict)
     =  20.063503

|          | ey/ex    | Std. Err. |     z  | P>|z|      | [95% C.I. ] |      X         |
|----------|----------|-----------|-------|---------|------------|-------------|
| stafcder | -1.038711| .41144    | -2.52 | 0.012   | -1.84511   | -.232307    | 1296.46     |
| subyear  | -.50.26422| .26882    | -1.87 | 0.062   | -1.022953  | 2.42444     | 1988.93     |
Cox proportional hazards estimates, STAFCDER with full battery of firm fixed effects, time trend and order of market entry

NOTICE THAT COEFFICIENTS, MARGINAL EFFECTS AND ELASTICITIES ARE ALL PRESENTED IN HAZARD FORM, SO POSITIVE COEFFICIENT MEANS INCREASE IN APPROVAL PROBABILITY AND REDUCTION IN APPROVAL TIME.

Cox regression -- Breslow method for ties

No. of subjects =          843                     Number of obs   =       843
No. of failures =          523
Time at risk    =  36292.47129
LR chi2(56)     =    459.42
Log likelihood  =   -2925.5154                     Prob > chi2     =    0.0000

------------------------------------------------------------------------------
  _t |   Haz. Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  stafcder |   1.002054    .000475     4.33   0.000     1.001123    1.002986
  subyear  |   1.023069   .0199427     1.17   0.242     .9847192    1.062912
FMX* Suppressed

. mfx compute, dydx
Marginal effects after cox
  y  = relative hazard (predict)
   =  24.079434

------------------------------------------------------------------------------
  variable |   dy/dx    Std. Err.     z    P>|z|   [95% C.I. ]      X
-------------+-----------------------------------------------------------------
  stafcder |   .059088   .018660   3.17   0.002   .022522  .095654   1296.46

. mfx compute, eyex
Elasticities after cox
  y  = relative hazard (predict)
   =  24.079434

------------------------------------------------------------------------------
  variable |    ey/ex    Std. Err.     z    P>|z|   [95% C.I. ]      X
-------------+-----------------------------------------------------------------
  stafcder |  3.181358   .240233  13.24   0.000   2.71051   3.6522   1296.46

THE COX MODEL IN STATA DOES NOT ALLOW FOR FRAILTIES/HETEROGENEITY
Lognormal results with controls for FDA Drug Priority Ratings
(firm fixed effects, shared frailties by primary indication, etc)

. streg stafcder subyear ratlp ratia ratlb ratlac ratiaa fmx*, dist(logn) frail
> ty(invga) shared(discode)

Log-normal regression --
accelerated failure-time form
Inverse-Gaussian shared frailty
Number of obs = 701
Number of groups = 179
Group variable: discode

No. of subjects = 701 Obs per group: min = 1
No. of failures = 521 avg = 3.916201
Time at risk = 20041.97261 max = 59

Log likelihood = -582.0334

------------------------------------------------------------------
|       Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+---------------------------------------------------------------
     _t |      Coef.   Std. Err.      z    P>|z|     [75% Conf. Interval]
-------------+---------------------------------------------------------------
stafcder |   -.0012245   .0002854    -4.29   0.000    -.0017838   -.0006651
subyear |   -.0550233   .0118149    -4.66   0.000    -.0781802   -.0318665
ratlp |   -.6396107   .0806674    -7.93   0.000    -.7977158   -.4815056
ratia |   -1.43886   .1498952    -9.60   0.000     -1.73265   -1.145071
ratlb |   -1.102453   .1346323    -8.21   0.000    -1.366088   -.8388176
ratlac |   -1.5293   .1265364    -12.56   0.000    -1.871004   -1.187596
ratiaa |   -4.506145   .3057475    -14.71   0.000    -5.093924   -3.918366
     _cons |   115.0242   23.25714     4.95   0.000     69.44105    160.6074
-------------+---------------------------------------------------------------
/ln_sig |   -.4798497   .0367459   -13.06   0.000    -.5518703   -.4078297
/ln_the |   -3.444204   1.996009    -1.73   0.084    -7.356309    .4679017
-------------+---------------------------------------------------------------
     sigma |   .6188764   .0227412          .6188764   .6188764
     theta |   .0319302   .0637329          .0319302   .0637329
-------------+---------------------------------------------------------------
Likelihood-ratio test of theta=0: chibar2(01) = 0.20 Prob>=chibar2 = 0.327

. mfx compute, dydx
Marginal effects after lnormalhet
 y  = predicted median _t (predict)
    = 23.840255

|         dy/dx   Std. Err.      z    P>|z|     [95% C.I.   ]     X
|---------------------------------------------------------------
stafcder |   -.0012245   .0002854    -4.29   0.000    -.0017838   -.0006651
subyear |   -.0550233   .0118149    -4.66   0.000    -.0781802   -.0318665
ratlp* |   -13.55721   1.68385    -8.01   0.000    -16.85357   -10.26085
ratia* |   -18.37371   1.68385    -10.91   0.000    -21.6739   -15.07351
ratlb* |   -18.37371   1.68385    -10.91   0.000    -21.6739   -15.07351
ratlac* |  -16.44649   2.20485    -7.466   0.000    -20.7679   -12.12511
ratiaa* |   -9.130688   4.22288    -2.16   0.031    -17.4072   -.8541612

. streg stafcder subyear ratlp ratia ratlb ratlac ratiaa fmx*, dist(logn) frail
> ty(invga) shared(discode)
LogNormal Model with PDUFA dummy variable (0 until 1992, 1 thereafter) and FDA Drug Priority Ratings. Full Battery of Firm Fixed Effects, Shared Frailties by Primary Indication, and Time Trend Control

. streg stafcder subyear pdufadum rat1p rat1a rat1b rat1c rat1aa fmx*, dist(log > n) frailty(inv) shared(discode)

note: fmxAkzoNobel dropped due to collinearity
note: fmxBiogen dropped due to collinearity
note: fmxPierreFabre dropped due to collinearity

Log-normal regression --
accelerated failure-time form
Inverse-Gaussian shared frailty
Number of obs = 701
Number of groups = 179
Group variable: discode

No. of subjects = 701 Obs per group: min = 1
No. of failures = 521 avg = 3.916201
Time at risk = 20041.97261 max = 59

Log likelihood = -581.35323 Prob > chi2 = 0.0000
------------------------------------------------------------------------------
    _t |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  stafcder |  -.0009819   .0003532    -2.78   0.005    -.0016742   -.0002896
  subyear  |  -.0544363   .0118071    -4.61   0.000    -.0775779   -.0312947
  pdufadum |  -.1528813   .1310265    -1.17   0.243    -.4096885    .1039259
  rat1p    |  -.6434245   .0806409    -7.98   0.000    -.8014778   -.4853711
  rat1a    |  -1.435447   .1496885    -9.59   0.000    -1.728831   -1.142063
  rat1b    |  -1.021378   .1338839    -7.63   0.000    -1.283786   -.7589707
  rat1c    |  -1.407102    .1255952    -5.95   0.000    -1.660781   -.1535158
  rat1aa   |  -.4602798   .3063838    -1.50   0.133    -1.060781    .1402214
    _cons  |   113.5953   23.25169     4.89   0.000     68.02281    159.1678
-------------+----------------------------------------------------------------
   /ln_sig   |  -.4813204   .0368744    -13.05   0.000    -.5535928   -.4090480
   /ln_the   |  -3.401976   1.933771    -1.76   0.079    -7.192098    .3881465
-------------+----------------------------------------------------------------
    sigma   |   .6179669   .0227871     27.05   0.000     .5748806    .6642823
    theta   |   .033074    .0644089     0.51   0.612     .0007525    1.474246
-------------+----------------------------------------------------------------
Likelihood-ratio test of theta=0: chibar2(01) = 0.21 Prob>chibar2 = 0.322
LogNormal Model with FirmSales x STAFCDER interaction, plus fixed effects and shared frailties.

IN THE FOLLOWING:

\textit{salereal\_defl1000} = SALES OF SUBMITTING FIRM IN SUBMISSION YEAR OF NME, DEFLATED AND DIVIDED BY MILLIONS OF U.S. 2000 DOLLARS

\textit{staff8f\_sales\_defl1000} = STAFCDER * salereal\_defl1000

. streg stafcder salereal\_defl1000 staff8f\_sales\_defl1000 fmx*, dist(logn) frai > lty(invg) shared(discode)

Note:
- fmxAkzoNobel dropped due to collinearity
- fmxBiogen dropped due to collinearity
- fmXMallinckrodt dropped due to collinearity
- fmXPierreFabre dropped due to collinearity

Log-normal regression --
accelerated failure-time form
Number of obs = 447
Inverse-Gaussian shared frailty
Number of groups = 149
Group variable: discode

No. of subjects = 447
Obs per group: min = 1
No. of failures = 363
avg = 3
Time at risk = 10784.41645
max = 37
LR chi2(56) = 161.24
Log likelihood = -401.0583
Prob > chi2 = 0.0000

------------------------------------------------------------------------------
_t | Coef. Std. Err. z P>|z| [95% Conf. Interval]
-------------+----------------------------------------------------------------
stafcder | -.001575 .0002249 -7.00 0.000 -.0020157 -.0011342
salereal\_1000 | -.0452584 .0267673 -1.69 0.091 -.0977213 .0072046
staff8f\_sales\_1000 | .0000311 .0000189 1.65 0.100 -5.92e-06 .0000682
_cons | 5.569758 .3462112 16.09 0.000 4.891196 6.248319
-------------+----------------------------------------------------------------
/ln\_sig | -.5103173 .0482474 -10.58 0.000 -.6048805 -.4157541
/ln\_the | -1.902325 .5795843 -3.28 0.001 -3.03829 -.7663611
-------------+----------------------------------------------------------------
sigma | .6003051 .0289632 20.76 0.000 .5424254 .6581848
theta | .1492212 .0864863 1.72 0.086 .0448944 .2535481
-------------+----------------------------------------------------------------
Likelihood-ratio test of theta=0: chibar2(01) = 5.86 Prob>=chibar2 = 0.008

---
LogNormal Model with Epidemiological and Political Covariates, Inverse Gaussian Frailties (Shared by Primary Indication), Fixed Firm Effects, plus time trend and other controls

```
. streg stafcder subyear prevgenx lethal deathrt1 hosp01 hospdisc hhosleng acut > ediz femdiz01 mandiz01 peddiz01 orphdum natreg wpnoavg3 orderent fmx*, dist(l > ogn) frailty(invg) shared(discode)
```

Note: fmxAkzoNobel dropped due to collinearity
Note: fmxBiogen dropped due to collinearity
Note: fmxGenzyme dropped due to collinearity
Note: fmxMylan dropped due to collinearity
Note: fmxNovoNordisk dropped due to collinearity
Note: fmxPierreFabre dropped due to collinearity
Note: fmxTEVA dropped due to collinearity
Note: fmxZambon dropped due to collinearity

Log-normal regression -- accelerated failure-time form
Number of obs = 450
Inverse-Gaussian shared frailty
Number of groups = 87
Group variable: discode
No. of subjects = 450
Obs per group: min = 1
No. of failures = 296
avg = 5.172414
Time at risk = 20829.23837
max = 78
LR chi2(63) = 214.08
Log likelihood = -465.50959
Prob > chi2 = 0.0000

|      | Coef.   | Std. Err. | z     | P>|z|  |   [95% Conf. Interval]   |
|------|---------|-----------|-------|------|----------------------------|
| stafcder | -.0033316 | .0005986 | -5.57 | 0.000 | -.0045049                 |
| subyear | .0701404  | .0272355 | 2.58  | 0.010 | .0167599                  |
| prevgnx | .001934   | .0006239 | 3.10  | 0.002 | .000711                   |
| lethal  | -.0385211 | .1817948 | -0.21 | 0.832 | -.3948324                 |
| deathrt1| -.3779325 | .1819253 | -2.08 | 0.038 | -.7344959                 |
| hosp01  | -.0262252 | .2224424 | -0.12 | 0.906 | -.4622043                 |
| hospdisc| 8.79e-07  | 4.82e-07 | 1.82  | 0.068 | -6.56e-08                 |
| hhosleng| .0266771  | .0170082 | 1.58  | 0.114 | .0002127                  |
| acutediz| -.2144682 | .0169756 | -1.27 | 0.204 | -.456542                  |
| femdiz01| -.129141  | .2708761 | -0.48 | 0.634 | -.6600484                 |
| mandiz01| -.3190436 | .3739797 | -0.85 | 0.394 | -.1.05203                 |
| peddiz01| .6582589  | .3919559 | 1.68  | 0.093 | .1.099605                 |
| orphdum | -.2385158 | .1527015 | -1.56 | 0.118 | -.5378053                 |
| natreg  | .0048876  | .0023794 | 2.05  | 0.040 | .0002241                  |
| wpnoavg3| -.0008318 | .0006582 | -1.26 | 0.206 | -.002129                  |
| orderent| .0093892  | .0063597 | 1.44  | 0.151 | -.0034284                 |
| _cons   | -131.4016 | 53.44383 | 2.46  | 0.014 | -236.1496                 |

/ln_sigma = -23.26355  .0671761  -3.46  0.001  -.3642982  -.1009728
/ln_theta = -1.411016  .731406  -1.93  0.054  -2.844546  .0225132

sigma = .7924424  .0532332  1.69  0.048  .694684  .9039576
theta = .2438953  .1783865  1.38  0.165  .0581607  1.022769

Likelihood-ratio test of theta=0: chibar2(01) = 5.75 Prob->chi2 = 0.008

. mfx compute, dydx
Marginal effects after lnormalhet
y = predicted median _t (predict)
= 24.679092

<p>|  | dy/dx | Std. Err. | z     | P&gt;|z|  |   [95% C.I. ]   |
|---|-------|-----------|-------|------|----------------------------|
|  |       |           |       |      |                           |</p>
<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>t-value</th>
<th>p-value</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
<th>Upper 95% Confidence Interval</th>
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<td>stafcdex</td>
<td>-0.0677</td>
<td>0.0190</td>
<td>-3.56</td>
<td>0.000</td>
<td>-0.1050</td>
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<td>0.7351</td>
<td>1.50</td>
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<td>-0.3400</td>
<td>2.5413</td>
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<td>0.138</td>
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<td>5.5111</td>
<td>-0.22</td>
<td>0.823</td>
<td>-12.03</td>
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<td>5.7514</td>
<td>-0.71</td>
<td>0.479</td>
<td>-15.34</td>
<td>7.2012</td>
<td>935.63</td>
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<tr>
<td>hosp01*</td>
<td>-0.9490</td>
<td>6.7817</td>
<td>-0.14</td>
<td>0.889</td>
<td>-14.20</td>
<td>14.97</td>
<td>373.33</td>
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<td>0.0001</td>
<td>1.99</td>
<td>0.047</td>
<td>3.5e-07</td>
<td>0.0005</td>
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<td>0.4819</td>
<td>-1.02</td>
<td>0.307</td>
<td>-1.43</td>
<td>1.43</td>
<td>452.68</td>
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<td>7.4439</td>
<td>0.05</td>
<td>0.958</td>
<td>-14.20</td>
<td>14.97</td>
<td>373.33</td>
</tr>
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<td>-2.9717</td>
<td>6.8303</td>
<td>-0.44</td>
<td>0.664</td>
<td>-16.36</td>
<td>12.63</td>
<td>935.63</td>
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<td>mandiz01*</td>
<td>-3.7873</td>
<td>8.3760</td>
<td>-0.45</td>
<td>0.651</td>
<td>-20.20</td>
<td>12.63</td>
<td>935.63</td>
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<td>24.06</td>
<td>0.99</td>
<td>0.323</td>
<td>-23.35</td>
<td>70.96</td>
<td>373.33</td>
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<td>orphdum*</td>
<td>-3.9615</td>
<td>3.6774</td>
<td>-1.08</td>
<td>0.281</td>
<td>-11.17</td>
<td>3.24</td>
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<td>12.447</td>
<td>0.90</td>
<td>0.366</td>
<td>-13.14</td>
<td>35.65</td>
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<td>1.19</td>
<td>0.234</td>
<td>-7.84</td>
<td>32.09</td>
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<td>25.111</td>
<td>0.48</td>
<td>0.633</td>
<td>-37.23</td>
<td>61.21</td>
<td>373.33</td>
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<td>durology*</td>
<td>11.6587</td>
<td>14.531</td>
<td>0.80</td>
<td>0.422</td>
<td>-16.82</td>
<td>40.13</td>
<td>777.78</td>
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<td>17.805</td>
<td>0.84</td>
<td>0.401</td>
<td>-19.94</td>
<td>49.86</td>
<td>355.56</td>
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<td>natreg</td>
<td>0.0577</td>
<td>0.0802</td>
<td>0.72</td>
<td>0.472</td>
<td>-0.0995</td>
<td>0.2187</td>
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<td>-1.00</td>
<td>0.320</td>
<td>-0.0602</td>
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<td>orderent</td>
<td>0.0320</td>
<td>0.2008</td>
<td>0.16</td>
<td>0.873</td>
<td>-3.6166</td>
<td>4.2571</td>
<td>10.549</td>
</tr>
</tbody>
</table>

(*) dy/dx is for discrete change of dummy variable from 0 to 1
. streg stafcder subyear prevgexn lethal deathrt1 hosp01 hospdisc hhosleng acut
> ediz femdiz01 mandiz01 peddiz01 orphdum natreg wpnoavg3 orderent fsubmits fmx
> *, dist(logn) frailty(invg) shared(discode)

note: fmxAkzoNobel dropped due to collinearity
...note: fmxZambon dropped due to collinearity

Log-normal regression --
accelerated failure-time form
Inverse-Gaussian shared frailty
Number of obs      =       348
Number of groups   =        86

Group variable: discode
No. of subjects =          348                  Obs per group: min =         1
No. of failures =          290                                 avg =  4.046512
Time at risk    =  9981.238352                                 max =        47
Log likelihood  =   -348.02838                  Prob > chi2        =    0.0000
------------------------------------------------------------------------------
   _t |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
   stafcder |  -.0023909   .0005069    -4.72   0.000    -.0033843   -.0013975
   subyear  |   .0432303   .0239753     1.80   0.071    -.0037605    .0902211
  prevgexn  |   .0015101   .0005795     2.61   0.009     .0003744    .0026458
    lethal  |   .0002638   .1649605     0.00   0.999    -.3230528    .3235804
deathrt1   |  -.1205568   .1485724    -0.81   0.417    -.4117533    .1706398
    hosp01  |   .0553999   .2097829     0.26   0.792     -.355767    .4665667
   hospdisc |   7.99e-07   .699e-07     0.00   0.999     .699e-07    .699e-07
   hhosleng |  -.0429822   .0162014    -2.65   0.008    -.0747363    -.011228
  acutediz  |  -.151759   .1474433    -1.03   0.303    -.4407426    .1372245
    femdiz01|  -.1524103   .2379233    -0.64   0.522     -.618731    .3151103
    mandiz01|  -.1633682   .3195515    -0.51   0.609     -.789677    .4630416
    peddiz01|   .3963856   .3591297     1.10   0.270     -.307495    1.100267
     orphdum|   .0591442   .1284041     0.46   0.645     -.192523    .3108117
   natreg   |   .0049175   .0020634     2.38   0.017     .0008733    .0089617
  wpnoavg3  |  -.0011352   .0006171    -1.84   0.066    -.0023446    .0000742
   orderent |   .0176731   .0056944     3.10   0.002     .0065122     .028834
  fsubmits  |   .0018117   .0147951    -0.12   0.901    -.0287995    .0324229
   _cons    |  -79.71792   47.10353    -1.69   0.091    -.172.0391    12.60331
-------------+----------------------------------------------------------------
   /ln_sig   |  -.4238354    .062762    -6.75   0.000    -.5468467   -.3008241
   /ln_the   |  -1.154004   .6811368   -1.69   0.090    -.2489008    .1809994
-------------+----------------------------------------------------------------
      sigma   |   .6545316   .0410797     64.77   0.000     .578772    .740208
      theta   |   .3153715   .2148111     1.48   0.140     -.082992    .7136345
------------------------------------------------------------------------------
Likelihood-ratio test of theta=0: chibar2(01) =     5.99 Prob>=chibar2 = 0.007

. mfx compute, dydx
Marginal effects after lnormalhet
y  = predicted median _t (predict)
   = 21.211912
------------------------------------------------------------------------------
  variable |      dy/dx    Std. Err.     z    P>|z|  [         95% C.I.        ]  X 
-------------+-----------------------------------------------------------------
   stafcder  |  -.0439477   .0114021   -3.85   0.000  -.066295  -.021600   1359.65
   _cons    |  -.0797921   .0471035   -1.69   0.091  -.172.0391    12.60331
------------------------------------------------------------------------------
 . mfx compute, eyex
Elasticities after lnormalhet
y  = predicted median _t (predict)
   = 21.211912
------------------------------------------------------------------------------
  variable |      ey/ex    Std. Err.     z    P>|z|  [         95% C.I.        ]  X 
-------------+-----------------------------------------------------------------
   stafcder  |  -2.816978   .7073113   -3.98   0.000  -4.203277  -1.430683   1359.65
------------------------------------------------------------------------------
LogNormal Model with Epidemiological and Political Covariates, Inverse Gaussian Frailties (Shared by Submitting Firm), plus time trend and other controls

```
. streg stafcder subyear prevgenx lethal deathrt1 hosp01 hospdisc hhosleng acut>
ediz femdiz01 mandiz01 peddiz01 orphdum natreg wpnoavg3 orderent, dist(logn)>
> frailty(invg) shared(firmcode)
```

Log-normal regression -- accelerated failure-time form

| Coefficient | Standard Error | z | P>|z| | 95% C.I. |
|-------------|----------------|---|------|---------|
| stafcder    | -0.0021069     | 0.0005127 | -4.11 | 0.000 | -0.0031117 -0.0011021 |
| subyear     | 0.0291715      | 0.0233203 | 1.25  | 0.211 | -0.0165355 0.0748785 |
| prevgenx    | 0.0014344      | 0.0004199 | 3.42  | 0.001 | 0.0006115 0.0022573 |
| lethal      | -0.160955      | 0.1197563 | -1.34 | 0.179 | -0.395673 0.073763  |
| deathrt1    | -0.1167153     | 0.1236353 | -0.94 | 0.345 | -0.359036 0.1256054 |
| hosp01      | 0.099901       | 0.1556945 | 0.64  | 0.521 | -0.2052545 0.4050566 |
| hospdisc    | 8.82e-07       | 3.41e-07  | 2.58  | 0.010 | 2.13e-07 1.55e-06  |
| hhosleng    | -0.0343216     | 0.0125586 | -2.73 | 0.006 | -0.0589359 -0.0097073 |
| acutediz    | -0.3325538     | 0.145099  | -2.90 | 0.004 | -0.5569891 -0.108186 |
| femdiz01    | -0.2417569     | 0.1942864 | -1.24 | 0.213 | -0.6225512 0.190374  |
| mandiz01    | 0.0329728      | 0.2455123 | 0.13  | 0.893 | -0.4482224 0.5141679 |
| peddiz01    | 0.1279047      | 0.2841728 | 0.45  | 0.653 | -0.4290638 0.6848732 |
|orphdum     | 0.0482062      | 0.1257939 | 3.78  | 0.000 | -0.20497 0.3013823 |
|natreg      | 0.0087556      | 0.0004093 | 2.07  | 0.038 | 0.0007215 0.0007891 |
|orderent    | -0.0047835     | 0.01264    | -3.78 | 0.000 | -0.07261 -0.02306 1304.25 |

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```
| variable    | ey/ex    | Std. Err. | z    | P>|z|  | [ 95% C.I. ] | X      |
|-------------|----------|-----------|------|-------|----------------|--------|
| stafcoder   | -2.747918 | .66864    | -4.11 | 0.000 | -4.05843 -1.43741 | 1304.25|
| subyear     | 58.03952  | 46.398    | 1.25 | 0.211 | -32.899 148.978  | 1989.6 |
| prevgenx    | .1643555  | .04811    | 3.42 | 0.001 | .070068 .258643  | 114.58 |
| lethal      | -.1013154 | .07538    | -1.34 | 0.179 | -.249062 .046431  | 629464 |
| deathrt1    | -.011039  | .01169    | -0.94 | 0.345 | -.033958 .01188  | 094581 |
| hosp01      | .0798316  | .12442    | 0.64 | 0.521 | -.16402 .323684  | 799107 |
| hospdisc    | .1180027  | .04566    | 2.58 | 0.010 | .028519 .207487  | 133765 |
| hhosleng    | -.179941  | .06584    | -2.73 | 0.006 | -.308989 -.050893 | 5.24279|
| acutediz    | -.1247077 | .04294    | -2.90 | 0.004 | -.208871 -.040544 | .375   |
| femdiz01    | -.0113324 | .00911    | -1.24 | 0.213 | -.029182 .006517  | 046875 |
| mandiz01    | .0008832  | .00658    | 0.13 | 0.893 | -.012006 .013772  | 026786 |
| peddiz01    | .0042825  | .00951    | 0.45 | 0.653 | -.014366 .022931  | 033482 |
| orphdum     | .0055954  | .01499    | 0.37 | 0.709 | -.023791 .034982  | 116071 |
| natreg      | .064857   | .02673    | 2.43 | 0.015 | .012461 .117254  | 16.7455|
| wpnoavg3    | -.0546636 | .0277     | -1.97 | 0.048 | -.108959 -.000368 | 67.7176|
| orderent    | .0926373  | .04877    | 1.90 | 0.058 | -.00295 1.88225  | 10.5804|

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

. mfx compute, eyex
LogNormal Model with Firm Covariates (Sales, Lobbying and Previous Submissions), with Firm Fixed Effects, and Inverse Gaussian Frailties (Shared by Primary Indication).

```
. streg stafcdor orphdum orderent fsubmits lnlobtot lnrsales_deflated fmx*, dis > t(logn) frailty(invg) shared(discode)
```

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

```
. note: fmxAkzoNobel dropped due to collinearity
note: fmxBiogen dropped due to collinearity
note: fmxMallinckrodt dropped due to collinearity
note: fmxPierreFabre dropped due to collinearity
```

Log-normal regression --
accelerated failure-time form
Number of obs = 414
Inverse-Gaussian shared frailty
Number of groups = 144
Group variable: discode
No. of subjects = 414
Obs per group: min = 1
No. of failures = 347
avg = 2.875
Time at risk = 10124.61371
max = 37
LR chi2(59) = 158.07
Log likelihood = -372.1706
Prob > chi2 = 0.0000

```
| _t         | Coef.  | Std. Err. | z     | P>|z| | [95% Conf. Interval] |
|------------|--------|-----------|-------|------|----------------------|
| stafcdor   | -0.0013053 | 0.0002221 | -5.88 | 0.000 | -.0017405 to -.00087 |
| orphdum    | -0.1188736 | 0.1103174 | -1.08 | 0.281 | -.3350918 to .0973445 |
| orderent   | 0.0165905 | 0.0051607 | 3.21  | 0.001 | .0064757 to .0267053 |
| fsubmits   | -0.0140588 | 0.0135953 | -1.03 | 0.301 | -.0407051 to .0125873 |
| lnlobtot   | -0.001778 | 0.0227944 | -0.08 | 0.938 | -.0464543 to .0428983 |
| lnrsales_d~d | -0.0375268 | 0.0222667 | -1.69 | 0.092 | -.0811687 to .0061151 |
| fmx3M      | -0.4277318 | 0.3393242 | -1.26 | 0.208 | -.1093757 to .2382938 |
| fmxAbbott  | -0.5829792 | 0.2862014 | -2.04 | 0.042 | -.1413924 to -.2203043 |
| fmxAcon    | 0.0318754 | 0.4544415 | 0.07  | 0.944 | -.8588135 to .9225643 |
| fmxAllergan| 1.552303  | 0.5378037 | 2.89  | 0.004 | .498227 to 2.606379  |
| fmxAmgen   | 2.503448  | 1.749819  | 1.43  | 0.153 | .342668 to 4.342877  |
| fmxAstamed-a| -1.49668 | 0.6434025 | -2.33 | 0.020 | -.257726 to 2.356344 |
| fmxAstra   | -0.453322 | 0.4454776 | -1.00 | 0.317 | -.821687 to .9140323 |
| fmxAvantis  | 0.1424753 | 0.36104   | 0.39  | 0.701 | -.5651501 to .8510017 |
| fmxBayer   | -0.0743627 | 0.2539426 | -0.94 | 0.349 | -.5450811 to .4503557 |
| fmxBoehr~n-z| -0.6882672 | 0.8439344 | -1.79 | 0.074 | -.1439684 to .6071099 |
| fmxBMS     | 0.1335807 | 0.3691019 | 0.36  | 0.716 | -.8628183 to .5843090 |
| fmxCibaGeigy| -0.3246168 | 0.2903523 | -1.12 | 0.266 | -.9317699 to .2825356 |
| fmxDuPont  | -0.0999926 | 0.6880505 | -0.15 | 0.881 | -.1409348 to 1.209362 |
| fmxEliLilly| -0.0617294 | 0.2659396 | -0.23 | 0.816 | -.5829613 to .4595026 |
| fmxFujisawa| -0.6209017 | 0.3685358 | -1.68 | 0.092 | -.1343219 to 1.01451 |
| fmxGenentech| 1.856666 | 3.234911  | 0.59  | 0.554 | -.6338452 to 3.342165 |
| fmxGenzyme | -0.4880675 | 0.4911998 | -0.99 | 0.320 | -.4.150801 to .4746664 |
| fmxGlaxo   | -0.4726448 | 0.2727791 | -1.73 | 0.083 | -1.007282 to .0619924 |
| fmxGlaxoW~e | -0.5026022 | 0.3815104 | -1.32 | 0.188 | -.1250349 to .2451443 |
| fmxHoecht  | 1.055117  | 0.3743514 | 0.28  | 0.778 | -.6281269 to .8391627 |
| fmxJohnson~n| 0.1395185 | 0.3745093 | 0.37  | 0.709 | -.5945061 to .8736341 |
| fmxMerck   | -0.392984 | 0.4224803 | -0.95 | 0.345 | -.1227344 to .4287478 |
| fmxSearle  | -1.0671822 | 0.7051697 | -1.51 | 0.130 | -.2.449289 to .3149252 |
| fmxMylan   | -0.8854287 | 0.6776736 | -1.33 | 0.183 | -.2.159645 to .4967873 |
| fmxNovartis| 1.1559809 | 0.4714178 | 0.27  | 0.790 | -.7983811 to 1.049543 |
| fmxNovonok~r| -0.8940566 | 0.6155505 | -1.42 | 0.157 | -.2.131873 to .3437596 |
| fmxOno     | 2.94804 | 10.30786 | 0.00 | 0.998 | -.2017356 to 2.023253 |
| fmxOrganon | -1.9296933 | 0.2857955 | -0.68 | 0.500 | -.7531182 to .3671796 |
| fmxOtsuka  | 0.151988 | 0.5790661 | 0.26  | 0.793 | -.9830299 to 1.286888 |
| fmxPfizer  | 0.261968 | 0.4031922 | 0.50  | 0.615 | -.5874224 to .993062 |
| fmxPharma~n| 0.0571833 | 0.3714392 | 0.08  | 0.933 | -.8337588 to .6225562 |
| fmxProctor~e| 0.5599248 | 0.4390529 | 1.28  | 0.202 | -.3006031 to 1.420453 |
| fmxRhone   | -0.2691112 | 0.4212503 | -0.64 | 0.523 | -.1.094747 to .5565242 |
```
| fmxRoche | -0.0807772 | 0.3763687 | -0.21 | 0.830 | -0.8184462 | 0.6568919 |
| fmxSandoz | -0.1506878 | 0.2695957 | -0.56 | 0.576 | -0.6790858 | 0.3777101 |
| fmxSankyo | -0.9262604 | 0.5357003 | -1.72 | 0.086 | -1.9821133 | 0.1995925 |
| fmxSanofi | -0.6567411 | 0.3061557 | -2.14 | 0.032 | -1.2568545 | 0.0562828 |
| fmxSchering | -0.0898143 | 0.6324131 | -0.14 | 0.887 | -1.3293215 | 0.1496933 |
| fmxScherin~h | 0.5722593 | 0.4083811 | 1.40 | 0.161 | -0.2281509 | 1.372669 |
| fmxSearle2 | -0.3188394 | 0.6351753 | -0.50 | 0.616 | -0.7405081 | 0.2620374 |
| fmxSKB | -0.2989702 | 0.3715357 | -0.80 | 0.421 | -1.0271671 | 0.4292264 |
| fmxSolvay | -0.3503266 | 0.4543722 | -0.08 | 0.939 | -1.2558537 | 0.8555201 |
| fmxSyntex | -0.2258583 | 0.1629572 | -0.30 | 0.761 | -0.7405081 | 0.2620374 |
| fmxTakeda | -0.3472028 | 0.4891561 | -0.77 | 0.439 | -1.2270615 | 0.5326555 |
| fmxTEVA | -0.0643297 | 0.6873657 | -0.09 | 0.925 | -0.1415425 | 1.282882 |
| fmxUCB | -0.4800962 | 0.6646247 | -0.72 | 0.470 | -1.7827375 | 0.8225443 |
| fmxUpjohn | -0.3401047 | 0.4567050 | -0.74 | 0.457 | -1.2353215 | 0.5511044 |
| fmxWarnerL~t | -0.1237663 | 0.5379929 | -0.32 | 0.747 | -0.8760088 | 0.6284562 |
| fmxBurroughs | -0.5524686 | 0.2620644 | -2.09 | 0.037 | -1.0770027 | 0.0349199 |
| fmxWyethAy~t | -0.3305463 | 0.2620644 | -1.26 | 0.208 | -1.8412711 | 0.8452196 |
| fmxZambon | -0.3453084 | 0.6316715 | 0.55 | 0.585 | -0.8927455 | 1.583362 |
| fmxZeneca | -0.2725643 | 0.4189896 | -0.65 | 0.515 | -1.0937863 | 0.5486582 |

_**_cons | 5.2084667 | 0.3583777 | 14.53 | 0.000 | 4.5060618 | 5.910873 |

/ln_sigg | -0.5350573 | 0.0491528 | -10.88 | 0.000 | -6.3141465 | -4.4387 |
/ln_the | -1.2801544 | 0.0686133 | -2.14 | 0.032 | -2.1951965 | -3.651329 |

sigma | 0.5856357 | 0.2079195 | 0.51 | 0.515 | 0.31389 | 0.6448742 |

theta | 0.2779917 | 0.1297835 | 0.11 | 0.515 | 0.1133681 | 0.6941044 |

Likelihood-ratio test of theta=0: chibar2(01) = 9.88 Prob>chibar2 = 0.001
Check on Influence of Outliers. Exclude obs > 99th Percentile of Sample, Re-Estimate LogNormal Model

```
. tabstat acttime, s(mean sd p1 p10 p90 p99)

<table>
<thead>
<tr>
<th>variable</th>
<th>mean</th>
<th>sd</th>
<th>p1</th>
<th>p10</th>
<th>p90</th>
<th>p99</th>
</tr>
</thead>
<tbody>
<tr>
<td>acttime</td>
<td>42.64</td>
<td>50.62</td>
<td>1.22</td>
<td>6.02</td>
<td>108.03</td>
<td>216.13</td>
</tr>
</tbody>
</table>
```

```
. streg stafcder subyear if(acttime < 216), dist(logn) frailty(invg) shared(dis>code)
```

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

Fitting comparison lnormal model:

```
Log-normal regression --
accelerated failure-time form  Number of obs      =       834
Inverse-Gaussian shared frailty Number of groups   =       180
Group variable: discode
No. of subjects =          834                  Obs per group: min =         1
No. of failures =          523                                 avg =  4.633333
Time at risk    =  34240.43839                                 max =        84
LR chi2(2)         =     93.87
Log likelihood  =   -905.47186                  Prob > chi2        =    0.0000
------------------------------------------------------------------------------
_t |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  stafcder |  -.0011877   .0003643    -3.26   0.001    -.0019018   -.0004737
  subyear  |  -.0120322   .0154153    -0.78   0.435    -.0422456   .0181812
  _cons    |   28.56371   30.22757     0.94   0.345    -30.68124    87.80866
-------------+----------------------------------------------------------------
 /ln_sig    |  -.2751687   .0480175    -5.73   0.000    -.3692812   -.1810561
 /ln_the   |  -.4179571   .2553905    -1.64   0.102    -.9185132     .082599
-------------+----------------------------------------------------------------
   sigma    |    .759444   .0364666                       .691231    .8343885
   theta    |   .6583905   .1681467                       .399112    1.086106
------------------------------------------------------------------------------
Likelihood-ratio test of theta=0: chibar2(01) = 143.99 Prob>chibar2 = 0.000
```

```
. mfx compute, dydx
Marginal effects after lnormalhet
 y  = predicted median _t (predict) =  21.933916
```

```
| variable  | dy/dx    | Std. Err. | z    | P>|z| | [    95% C.I.   | X     |
|------------|----------|-----------|-----|-----|-----------------|-------|
| stafcder   | -.0260516| .00829    | -3.14|  0.002| -.0422986 -.009805|1299.53|
| subyear    | -.263913 | .33871    | -0.78|  0.436| -.927771  .399945 |1989.01|
```

```
. mfx compute, eyex
Elasticities after lnormalhet
 y  = predicted median _t (predict) =  21.933916
```

```
| variable  | ey/ex    | Std. Err. | z    | P>|z| | [    95% C.I.   | X     |
|------------|----------|-----------|-----|-----|-----------------|-------|
| stafcder   | -1.543499| .47343    | -3.26|  0.001| -.24714 -.615598|1299.53|
| subyear    | -23.93218| 30.661    | -0.78|  0.435| -.840271  36.1627 |1989.01|
```
Baseline LogNormal Model for Comparison to Previous Page

```
. streg stafcder subyear, dist(logn) frailty(invg) shared(discode)
    failure _d: aprovdm
    analysis time _t: acttime

Log-normal regression --
    accelerated failure-time form          Number of obs      =       843
    Inverse-Gaussian shared frailty        Number of groups   =       180
Group variable: discode

No. of subjects =          843                  Obs per group: min =         1
No. of failures =          523                                 avg =  4.683333
Time at risk    =  36292.47129                                 max =        85

LR chi2(2)         =     95.41
Log likelihood  =   -918.89635                  Prob > chi2        =    0.0000

------------------------------------------------------------------------------
     _t |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     stafcder |   -.001141   .0003674    -3.11   0.002    -.0018611    -.000421
     subyear |  -.0153089   .0155053    -0.99   0.323    -.0456987    .0150809
     _cons |   35.01552   30.40358     1.15   0.249    -24.57441    94.60544
------------------------------------------------------------------------------
     /ln_sig |  -.2726315   .0487074    -5.60   0.000    -.3680961   -.1771668
     /ln_the |  -.3477697   .2523383    -1.38   0.168    -.8423436   .1468042
------------------------------------------------------------------------------
    sigma |   .7613733   .0370845                      .6920507    .8376401
    theta |   .7062615   .1782168                         .4307    1.158127
------------------------------------------------------------------------------

Likelihood-ratio test of theta=0: chibar2(01) =   155.51 Prob>=chibar2 = 0.000

. mfx compute, dydx
Marginal effects after lnormalhet
    y  = predicted median _t (predict)
        =  21.931525

variable |      dy/dx    Std. Err.     z    P>|z|  [    95% C.I.   ]      X  
---------+--------------------------------------------------------------------
    stafcder |   -.025024      .00833   -3.00   0.003  -.041358  -.00869   1296.46
    subyear |  -.3357476      .34125   -0.98   0.325  -1.00459  .333092   1988.93
---------+--------------------------------------------------------------------

. mfx compute, eyex
Elasticities after lnormalhet
    y  = predicted median _t (predict)
        =  21.931525

variable |      ey/ex    Std. Err.     z    P>|z|  [    95% C.I.   ]      X  
---------+--------------------------------------------------------------------
    stafcder |  -1.479271      .47629   -3.11   0.002  -2.41358  -.54575  1296.46
    subyear |  -30.44832      30.839   -0.99   0.323  -90.8915  29.9948  1988.93
---------+--------------------------------------------------------------------
```