Models In Epidemiology And Biostatistics
Gordon Hilton Fick

Slope - Ratio Assays

From Finney(1951). Data is in Finney_1951.dta

```
. regr resp dose td

      Source |       SS           df       MS      Number of obs   =        20
-------------+----------------------------------   F(2, 17)        =   1057.33
       Model |  31456.9143         2  15728.4571   Prob > F        =    0.0000
    Residual |  252.885714        17  14.8756303   R-squared       =    0.9920
-------------+----------------------------------   Adj R-squared   =    0.9911
       Total |     31709.8        19  1668.93684   Root MSE        =    3.8569

------------------------------------------------------------------------------
        resp |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        dose |   59.31429   1.303868    45.49   0.000     56.56336    62.06521
          td |      -18.7   1.219657   -15.33   0.000    -21.27325   -16.12675
       _cons |   42.14286   1.629835    25.86   0.000     38.70421    45.58151
------------------------------------------------------------------------------
```

Estimate and CI for the relative potency of the test relative to the standard using the 'delta method'.

```
. nlcom _b[td]/_b[dose]+1

       _nl_1:  _b[td]/_b[dose]+1

------------------------------------------------------------------------------
        resp |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _nl_1 |   .6847303   .0183725    37.27   0.000     .6487208    .7207397
------------------------------------------------------------------------------
```

The analysis of variance from Finney(1951)

```
. anova resp c.dose c.td blank test,seq

                          Number of obs =         20    R-squared     =  0.9932
                          Root MSE      =    3.79912    Adj R-squared =  0.9914

                     Source |    Seq. SS         df         MS        F    Prob>F
                ------------+------------------------------------------------------
                      Model |    31493.3          4    7873.325    545.50  0.0000
                            |
                       dose |  27960.014          1   27960.014   1937.18  0.0000
                         td |     3496.9          1      3496.9    242.28  0.0000
                      blank |  2.1607143          1   2.1607143      0.15  0.7043
                       test |     34.225          1      34.225      2.37  0.1444
                            |
                   Residual |      216.5         15   14.433333
                ------------+------------------------------------------------------
                      Total |    31709.8         19   1668.9368
```

An example with three preparations.
An in-vitro assay of influenza vaccines (European Pharmacopoeia 5th; 2005 p492).
Data is in slope_ratio.dta.

```
. regr resp dose td ud

      Source |       SS           df       MS      Number of obs   =        24
-------------+----------------------------------   F(3, 20)        =    339.56
       Model |  1087.66517         3  362.555058   Prob > F        =    0.0000
    Residual |  21.3543855        20  1.06771927   R-squared       =    0.9807
-------------+----------------------------------   Adj R-squared   =    0.9779
       Total |  1109.01956        23  48.2182417   Root MSE        =    1.0333

------------------------------------------------------------------------------
        resp |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        dose |   .8474815   .0290453    29.18   0.000      .786894    .9080689
          td |       -.04    .025154    -1.59   0.127    -.0924703    .0124703
          ud |  -.2977778    .025154   -11.84   0.000     -.350248   -.2453075
       _cons |   11.04167   .5166525    21.37   0.000     9.963948    12.11938
------------------------------------------------------------------------------


. nlcom _b[td]/_b[dose] +1

------------------------------------------------------------------------------
        resp |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _nl_1 |   .9528014   .0290171    32.84   0.000     .8959289    1.009674
------------------------------------------------------------------------------

. nlcom _b[ud]/_b[dose] +1

------------------------------------------------------------------------------
        resp |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _nl_1 |   .6486321   .0267662    24.23   0.000     .5961713     .701093
------------------------------------------------------------------------------
```

The analysis of variance [as in the report]

```
. anova resp c.dose c.td c.ud test unkn c.d2 c.td2 c.ud2 c.d3 c.td3 c.ud3, seq

                   Source |    Seq. SS         df         MS        F    Prob>F
                ----------+-----------------------------------------------------
                    Model |  1096.2046         11   99.654961     93.32  0.0000
                          |
                     dose |  911.35408          1   911.35408    853.39  0.0000
                       td |  26.677782          1   26.677782     24.98  0.0003
                       ud |  149.63331          1   149.63331    140.12  0.0000
                     test |  3.4672227          1   3.4672227      3.25  0.0967
                     unkn |  .00666665          1   .00666665      0.01  0.9383
                       d2 |  .00041665          1   .00041665      0.00  0.9846
                      td2 |  .04083348          1   .04083348      0.04  0.8482
                      ud2 |   .0400004          1    .0400004      0.04  0.8498
                       d3 |  .39675072          1   .39675072      0.37  0.5535
                      td3 |  4.5375039          1   4.5375039      4.25  0.0616
                      ud3 |  .05000005          1   .05000005      0.05  0.8323
                          |
                 Residual |  12.814991         12   1.0679159
                ----------+-----------------------------------------------------
```

```
       Total |  1109.0196         23   48.218242
```

Here is another example. Nonlinearity is noted. The analysts excluded the blanks [the zero doses]. See European Pharmacopoeia(5th, 2005, p 491) for more. Data is in slope_ratio_2.dta

```
. regr resp dose pd if blank==0

      Source |       SS           df       MS      Number of obs   =        48
-------------+----------------------------------   F(2, 45)        =  23311.46
       Model |  .191696634         2  .095848317   Prob > F        =    0.0000
    Residual |  .000185024        45  4.1116e-06   R-squared       =    0.9990
-------------+----------------------------------   Adj R-squared   =    0.9990
       Total |  .191881658        47  .004082588   Root MSE        =    .00203

------------------------------------------------------------------------------
        resp |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        dose |   .0822411   .0003832   214.62   0.000     .0814693    .0830129
          pd |  -.0145446    .000271   -53.68   0.000    -.0150904   -.0139989
       _cons |   .0529792   .0007743    68.42   0.000     .0514196    .0545388
------------------------------------------------------------------------------

. nlcom _b[pd]/_b[dose]+1

       _nl_1:  _b[pd]/_b[dose]+1

------------------------------------------------------------------------------
        resp |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _nl_1 |   .8231462   .0031008   265.47   0.000     .8170689    .8292236
------------------------------------------------------------------------------

. anova resp c.dose c.pd prep c.d2 c.pd2 if blank==0, seq

                          Number of obs =         48    R-squared     =  0.9992
                          Root MSE      =    .001964    Adj R-squared =  0.9991

                  Source |    Seq. SS         df         MS        F    Prob>F
              -----------+----------------------------------------------------
                   Model |  .19171966          5   .03834393   9941.02  0.0000
                         |
                    dose |  .17985002          1   .17985002  46627.79  0.0000
                      pd |  .01184661          1   .01184661   3071.34  0.0000
                    prep |  2.976e-09          1   2.976e-09      0.00  0.9780
                      d2 |  .00001426          1   .00001426      3.70  0.0613
                     pd2 |  8.760e-06          1   8.760e-06      2.27  0.1393
                         |
                Residual |    .000162         42   3.857e-06
              -----------+----------------------------------------------------
                   Total |  .19188166         47   .00408259
```