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John Furman, PhD
Department of Labor and Industries
Tumwater, WA

2 December, 2007

Dear Dr. Furman:

Pursuant to your request, I have completed an analysis of 2007 cholinesterase monitoring program data, to determine comparability to 2004-2006 data quality and to discern any trends in data quality. This analysis was done jointly by myself and Dr. Gerald van Belle, and relied on the following materials:

- Cholinesterase Rule Scientific Advisory Committee reports: 2004, 2005, and 2004-2006
- 2007 Cholinesterase monitoring data, that you provided to us in an excel spreadsheet

In addition, I reviewed laboratory records provided by the contract laboratory that performed the testing (Pathology Associates Medical Laboratories: PAML). These included a copy of the 1/16/2007 revision of the SOP that PAML uses, and QC data through August, 2007: control sample results and control charts, However, I did not attempt to audit the laboratory's procedures or practices directly (as I did for the Public Health Lab in 2004 and 2005). It is my understanding that L&I has arranged for experts in ChE measurement to assist in reviewing lab procedures and practices.

A final introductory point is to re-state that the nature of the cholinesterase assay makes the absolute values determined for a particular sample highly dependent on the lab and method used. It is not to be expected that ChE assay results would bear comparison between one year and another, especially when major changes in method or lab were involved. Ratios of ChE activities, calculated as "depression" results, should be much less method- and lab dependent. The range and average ChE activity (either RBC or serum) reported by PAML in 2007 do differ substantially from the equivalent numbers from the PHL in 2004-2006. The focus of our review was to compute those statistical indicators of data precision that we used in 2004-2006 for comparison to earlier results.

Emblem: a Northwest Coast Indian symbol of physical and mental well-being. Artist: Marvin Oliver

Within-lab QC data and external (blind) QC sample results: materials provided indicate that PAML makes routine use of control samples and other procedures to track method precision and accuracy. The within-lab results were not systematically reviewed, but appear to be comparable to similar indicators produced by PHL in prior years. The practice of recurring submission of blind QC samples (from unexposed individuals) was continued in 2007. As in prior years, we considered the replicate precision of the overall set of submissions as an index of within-lab variability (although effects of sample collection and shipment could also influence the precision of results). A total of 107 pairs of samples were reported; the overall precision of each assay expressed as a percent coefficient of variation was: 16.7% for RBC ChE (significantly less precise than in prior years) and 2.6% for serum ChE (reasonably comparable to precision in prior years). Table 1 shows the year-by-year comparision.

Table 1: Precision for RBC and serum ChE results, 2004-2007

	RBC ChE				Serum ChE			
	2004	2005	2006	2007	2004	2005	2006	2007
I. Replicate Precision: Blinded Field QC Samples								
N pairs	53	186	*88	107	53	176	*89	107
% CV	6.5%	4.2%	3.8%	16.7%	1.6%	2.1%	2.5%	2.6%
dates/person	1 or 2	up to 7	*up to 5	up to 6	1 or 2	up to 7	*up to 5	up to 6
II. Estimated Within-Person % CV from Monitoring Results								
(baseline vs first periodic test)								
% CV	9%	5.5%	4.3%	15.1%	10%	6.6%	8.3%	7.1%

**through 7/31/2006 only*

Overall system precision was also estimated from actual field data, as was done in each of the three prior years, using analysis of variance. In this approach, the pairwise comparison of baseline and periodic sample is adjusted for the overall effect between baseline and periodic test (depression), and the remaining (random) variation is used to estimate a within-person coefficient of variation. This index is somewhat more realistic as an indicator of the potential magnitude of random effects for calculated "depression" results, because it also includes random changes in ChE activity within a person over time. As was seen in prior years, the two approaches give fairly consistent results: for RBC, the within-person %CV was 15.1% (significantly less precise than in prior years), and serum assay gave a %CV of 7.1% (comparable to that seen in prior years). The detailed analysis performed by Dr. van Belle is attached as Appendix 1.

Time trends within the 2007 monitoring season were examined to see whether precision was changing over the course of the season (perhaps as the lab routines became more familiar). Comparison of mean and standard deviation for RBC ChE from baseline samples across the 8 observational periods shows only a hint of decreased variability, and no significant trend to higher or lower mean value. There is even less indication of a time trend for serum ChE. This would indicate that bias over time was not an important effect in the 2007 data.

Estimates of false positives and rate of actual depression: as in past years, we applied the estimates of variability to the number of tests and number of alerts reported in 2007, to assess the possible impact in terms of false negatives and false positives. The approach and example calculations are presented in detail in the 2004 and 2005 ChE report from the Scientific Advisory Committee. The results for 2007 are presented and compared with results from prior years in Table 2, below.

The observed within-person %CV for RBC in 2007 produced a 14.6% likelihood (at 95% confidence) of a RBC "depression" exceeding 20% for an unexposed person. Therefore, for 100 baseline/periodic test pairs, 14.6 would incorrectly trigger an alert, if none of the handlers tested had true depression. If there were some level of depression in the samples, then the number of false positives would be lower. Applied to the 510 periodic tests reported, up to 76 false positives could occur. This number exceeds the actual number of apparently positive tests at >20% depression. Therefore, the rate of "work practices" alerts for RBC ChE could be as low as zero after correction for random variation. At the 30% depression level, this pattern is repeated. The overall finding for RBC ChE is not qualitatively different than that seen in prior years, but the uncertainty in it is much larger. In prior years, the adjusted rate of RBC ChE depression was around 1 to 2% at the 20% level and 0 to 1% at the 30% level, but in 2007 the range would be as high as 13% (20% depression) or 4% (30 % depression), if one assumes no false positives.

In contrast, the serum ChE had false positive rates similar to those calculated for prior years. However, significantly fewer cases of apparent depression were seen in 2007, leading to lower adjusted rates of depression at both the 20% level and at the 40% level.

Table 2 - Alerts and false positives, 2004-2007

RBC ChE depression	2004 results		2005 results		*2006 results		2007 results	
	>20% depression	>30% depression	>20% depression	>30% depression	>20% depression	>30% depression	>20% depression	>30% depression
False Positive Rate	3.98%	0.25%	0.43%	0.0013%	0.012%	0%	14.6%	4.63%
Number, periodic tests	911	911	954	954	*692	*692	510	510
Observed positives	47	15	21	1	4	0	67	20
Estimated maximum number of false positives	≤ 35.80	≤2.28	≤4.03	≤0.01	≤0.10	<0.00	≤76.00	≤24.00
Adjusted rate of alerts**	1.3%	1.4%	≤1.8%	0.10%	0.6%	0%	**< 0 ****	**< 0 ****
Serum ChE depressio	>20% depression	>40% depression	>20% depression	>40% depression	>20% depression	>40% depression	>20% depression	>40% depression
False Positive Rate	5.73%	0.02%	1.21%	0.00001%	2.43%	0.0003%	1.21%	0.00001%
Number, periodic tests	911	911	954	954	*692	*692	510	510
Observed positives	155	29	86	12	96	12	24	2
Estimated maximum number of false positives	≤31.32	≤0.03	≤10.63	0	≤15.2	0	≤10	0
Adjusted rate of alerts**	≤14%	≤3%	≤8%	negligible	11.9%	1.7%	2.80%	0.39%

**through 7/31/2006 only*

*** potential number of false positives exceeds the number of observed positives*

The decreased precision for RBC compared with prior years also decreases the margin of safety regarding false negative results. In order to have a high probability of correctly classifying a test as triggering an alert, the true depression in the sample must exceed the

depression level that triggers the alert, to a degree that increases with the imprecision of the test. A handler with a true RBC ChE depression of 35% would have a 95% chance of having in a work practices alert and a 72% chance of having an exposure removal alert, if the overall precision of monitoring were 9 %CV, but at 15 %CV, the chances of alerts would be reduced to 84% (wp alert) and 64% (er alert). Viewed another way, in order for there to be 95% likelihood of recognizing a wp alert, a handler would need to have an actual RCB ChE depression of 44% in 2007 but only 28% in 2006.

In summary, we do not find indications of either bias or major seasonal drift according to the measures available to us. The serum ChE assay appears comparable in performance to that used in prior years, and the relatively lower rate of serum ChE depressions in 2007 does not appear to be an analytical artifact. The high variability of RBC ChE in 2007 deserves further attention, as it may prevent recognition of some cases of exposure, and lead to false alerts in other cases. In order to have an overall precision for RBC ChE of under 10%, the within-lab analytical precision needs to be well under that figure. This is a precision requirement that is more stringent than is usual for ChE measurements for clinical purposes, and the physical/chemical nature of RBC ChE makes achieving 5 – 10% CV for the analysis challenging. Past experience with this program suggests that tightening up this assay precision will take sustained effort, but is an achievable goal.

Yours,

Dave Kalman

Dave Kalman, PhD
Professor and Chair

2007 Che Analysis

Gerald van Belle

October 26, 2007

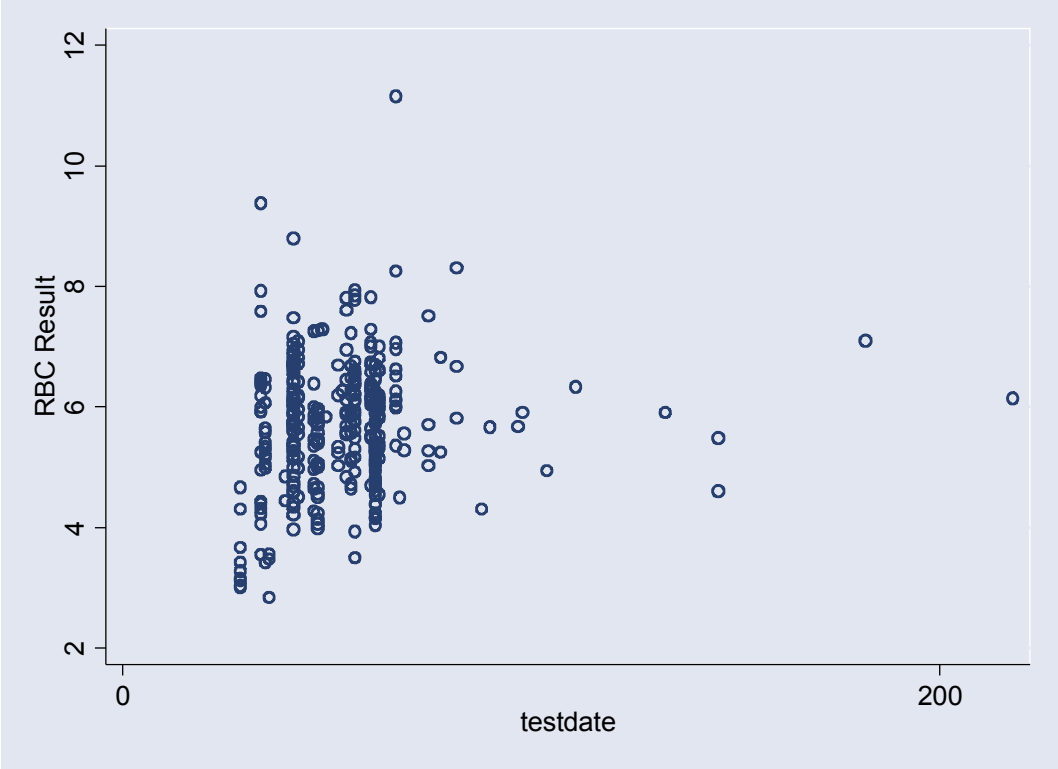
```
       log:  G:\Projects\CHeProject\2007 Analyses\2007.10.26 analysis.smcl
  log type:  smcl
 opened on:  26 Oct 2007, 20:45:40

. do "C:\DOCUME~1\HP_Owner\LOCALS~1\Temp\STD01000000.tmp"

. use "G:\Projects\CHeProject\2007 Analyses\Long File With Correct Dates (Includes
W).dta", clear

.
. sum

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   accession |      2252    7.00e+07     1327588    7000262   7.00e+07
  employeeid |      2252    1446.216    1394.019         12       9083
         dob |         0
monitoring~e |         0
  employerid |      2210    1994.367    1728.795       1001      20007
-------------+--------------------------------------------------------
datecollec~d |         0
datereceived |         0
tempofsamp~c |      2186     3.86688    3.686717          1         46
    rbcunits |         0
   rbcresult |      2250     5.69368    1.065979        2.7      11.14
-------------+--------------------------------------------------------
  serumunits |         0
 serumresult |      2252     11.6171    2.091235       3.36      19.25
dateofanal~s |         0
rbcpercent~e |       510   -.4787224    23.73916     -53.79      191.1
serumperce~e |       509   -5.519074    11.01209  -76.01713      23.91
-------------+--------------------------------------------------------
 hours30days |       283    39.22898    32.48593          0        240
  hourstotal |       244    70.39139    52.61991          0        336
    comments |         0
datereported |         0

. *drop if employeeid>5000
. drop if monitoringstage=="W"
(0 observations deleted)
. gsort -monitoringstage
. sort employeeid, stable
. gen number=_n
. bysort employeeid: gen obs=_n
. bysort employeeid: gen OBS=_N
. bysort obs: sum rbcresult serumresult

-------------------------------------------------------------------------------
-> obs = 1

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |      1747    5.718569    1.095875        2.7      11.14
 serumresult |      1749    11.80813    2.039118       4.43      18.78

-------------------------------------------------------------------------------
-> obs = 2

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |       352    5.644432    .9386571        3.6       9.49
 serumresult |       352    11.15267    2.031086       6.14      19.25

-------------------------------------------------------------------------------
-> obs = 3
```

```
    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |       103    5.547087    1.011648       3.01       7.94
 serumresult |       103    10.81146    2.255855       3.36      18.67

-------------------------------------------------------------------------------
-> obs = 4

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        26    5.500769     1.08383       3.33       8.01
 serumresult |        26        9.76    2.242361       3.42      13.53

-------------------------------------------------------------------------------
-> obs = 5

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        12    5.543333    .7168027       4.51       6.63
 serumresult |        12        9.38    2.131291       5.99      12.39

-------------------------------------------------------------------------------
-> obs = 6

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |         7        5.35    .4827008       4.56        5.9
 serumresult |         7    10.11571    2.973583       5.77      12.48

-------------------------------------------------------------------------------
-> obs = 7

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |         2       5.555    .1343503       5.46       5.65
 serumresult |         2      10.795    2.580939       8.97      12.62

-------------------------------------------------------------------------------
-> obs = 8

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |         1        4.15           .       4.15       4.15
 serumresult |         1       11.25           .      11.25      11.25


. tab OBS if obs==1

        OBS |      Freq.     Percent        Cum.
------------+-----------------------------------
          1 |      1,397       79.87       79.87
          2 |        249       14.24       94.11
          3 |         77        4.40       98.51
          4 |         14        0.80       99.31
          5 |          5        0.29       99.60
          6 |          5        0.29       99.89
          7 |          1        0.06       99.94
          8 |          1        0.06      100.00
------------+-----------------------------------
      Total |      1,749      100.00

. *total for OBS is the number of individuals in the data set*
. bysort OBS: sum rbcresult serumresult if obs==1

-------------------------------------------------------------------------------
-> OBS = 1

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |      1395    5.727355     1.11044        2.7      10.96
```

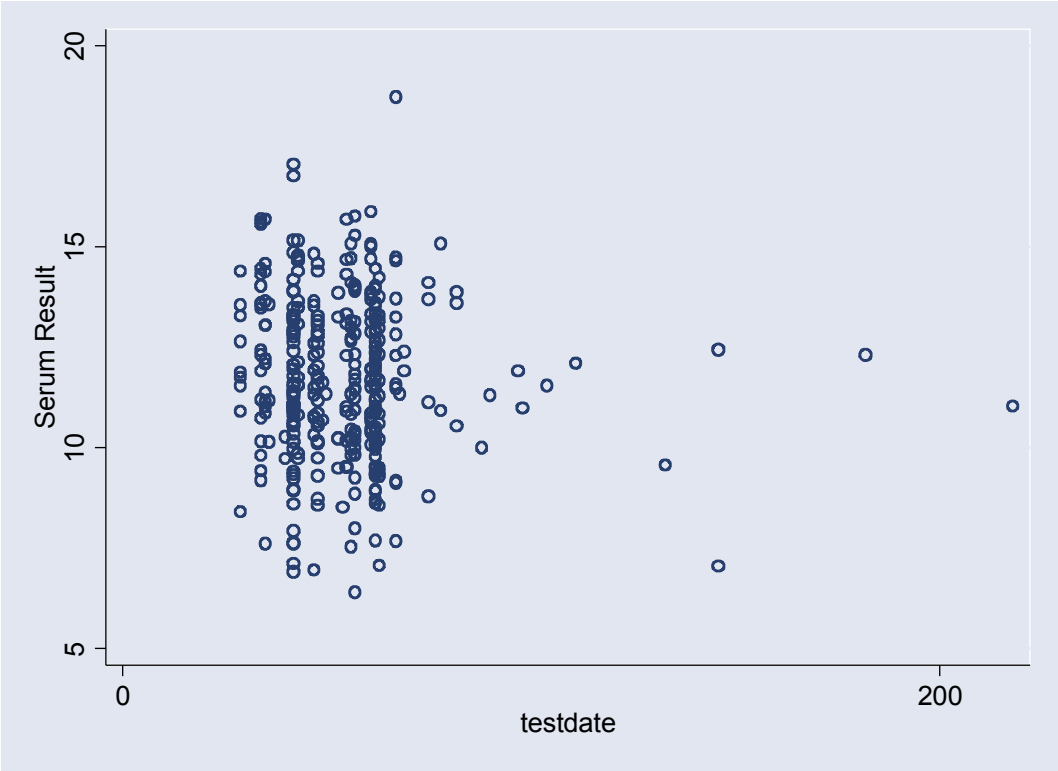
```
 serumresult |      1397    11.83429    2.047726       4.43      18.78

-------------------------------------------------------------------------------
-> OBS = 2

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |       249    5.571727    1.037749          3      11.14
 serumresult |       249    11.70217    2.033263       6.38      18.72

-------------------------------------------------------------------------------
-> OBS = 3

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        77    6.007273    .9342048       2.83       8.79
 serumresult |        77     11.7887    1.930439       7.92      17.04

-------------------------------------------------------------------------------
-> OBS = 4

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        14        5.99    1.309927        4.3       9.37
 serumresult |        14      12.035     1.76453       9.49      15.75

-------------------------------------------------------------------------------
-> OBS = 5

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |         5       5.372    .7691034        4.2       6.17
 serumresult |         5       9.718    1.911248       7.11      12.08

-------------------------------------------------------------------------------
-> OBS = 6

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |         5       5.346    .5904489       4.59       5.93
 serumresult |         5      11.378    2.373809       7.59      14.01

-------------------------------------------------------------------------------
-> OBS = 7

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |         1        5.54           .       5.54       5.54
 serumresult |         1       11.54           .      11.54      11.54

-------------------------------------------------------------------------------
-> OBS = 8

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |         1        7.77           .       7.77       7.77
 serumresult |         1       12.83           .      12.83      12.83


. gen testdate=date(dateofanalysis,"md20y")-17184
```

testdate is the day in year 2007. January 1, 2007 is day 1.
The purpose of these analyses is to assess whether the variability is decreasing over time. The evidence is minimal.

```
(5 missing values generated)

.twoway scatter rbcresult testdate if obs==1
```




```
.twoway scatter serumresult testdate if obs==1
```



I now split the test dates into 30 day intervals in order to calculate the mean and standard deviation in that period.

```
. gen testperiod=1

. replace testperiod=2 if testdate>30 & testdate<61
(1068 real changes made)

. replace testperiod=3 if testdate>60 & testdate<91
(675 real changes made)

. replace testperiod=4 if testdate>90 & testdate<121
(241 real changes made)

. replace testperiod=5 if testdate>120 & testdate<151
(70 real changes made)

. replace testperiod=6 if testdate>150 & testdate<181
(68 real changes made)

. replace testperiod=7 if testdate>180 & testdate<211
(60 real changes made)

. replace testperiod=8 if testdate>210 & testdate<241
(19 real changes made)

. tab testperiod

 testperiod |      Freq.     Percent        Cum.
------------+-----------------------------------
          1 |         51        2.26        2.26
          2 |      1,068       47.42       49.69
          3 |        675       29.97       79.66
          4 |        241       10.70       90.36
          5 |         70        3.11       93.47
          6 |         68        3.02       96.49
          7 |         60        2.66       99.16
          8 |         19        0.84      100.00
------------+-----------------------------------
      Total |      2,252      100.00
```

Here I use all the data including second and subsequent observations on an individual.

```
. bysort testperiod: sum rbcresult serumresult

-------------------------------------------------------------------------------
-> testperiod = 1

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        51    5.367255    2.001608       2.88       9.75
 serumresult |        51    11.76882    1.848819       5.52      15.57

-------------------------------------------------------------------------------
-> testperiod = 2

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |      1068    5.691227     1.12625        2.7      10.96
 serumresult |      1068    11.89237     2.12899       4.43      18.78

-------------------------------------------------------------------------------
-> testperiod = 3

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |       674    5.751068    .9855248       3.01      11.14
 serumresult |       675    11.62647    1.960622       5.67      18.72

-------------------------------------------------------------------------------
-> testperiod = 4
```

```
    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |       240    5.666375    .8535227       3.69       8.32
 serumresult |       241    11.00656    2.252949       3.36      19.25

-------------------------------------------------------------------------------
-> testperiod = 5

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        70    5.731571     .737669       4.35       7.88
 serumresult |        70    10.85486    2.155619       5.77       15.4

-------------------------------------------------------------------------------
-> testperiod = 6

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        68    5.859706    .9334465       4.46       8.36
 serumresult |        68    10.89574    1.654341       6.95      14.39

-------------------------------------------------------------------------------
-> testperiod = 7

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        60       5.073    .7121209       3.33       7.09
 serumresult |        60    10.74833    1.595972        6.3       13.2

-------------------------------------------------------------------------------
-> testperiod = 8

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        19    6.243158    .7278893       4.96       7.54
 serumresult |        19    11.28158    2.084483        7.7      14.77
```

Here I only use the first observation

```
. bysort testperiod : sum rbcresult serumresult if obs==1

-------------------------------------------------------------------------------
-> testperiod = 1

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        45    5.409111    2.106081       2.88       9.75
 serumresult |        45    11.98022     1.74771       5.52      15.57

-------------------------------------------------------------------------------
-> testperiod = 2

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |      1058    5.689839    1.128722        2.7      10.96
 serumresult |      1058    11.89289    2.131723       4.43      18.78

-------------------------------------------------------------------------------
-> testperiod = 3

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |       531    5.825424    .9302529       3.53      11.14
 serumresult |       532    11.73786    1.907841       5.67      18.72

-------------------------------------------------------------------------------
-> testperiod = 4
```

```
    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        48    5.592292    .8726098       3.69       7.55
 serumresult |        49     11.4251    1.805799       6.56      15.32

-------------------------------------------------------------------------------
-> testperiod = 5

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        34    5.477647    .6397161       4.35       7.52
 serumresult |        34    11.20324    1.993416       6.62       15.4

-------------------------------------------------------------------------------
-> testperiod = 6

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        14    6.182143    1.176064       5.05       8.36
 serumresult |        14    11.36714     1.36307       9.84      13.67

-------------------------------------------------------------------------------
-> testperiod = 7

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |        14    5.325714    .8479633       3.88       7.09
 serumresult |        14    10.79357      1.5471       6.86       13.2

-------------------------------------------------------------------------------
-> testperiod = 8

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
   rbcresult |         3           6    .4396589       5.51       6.36
 serumresult |         3        11.7    1.799111      10.34      13.74
```

These analyses are used to calculate the within-subject variability, which is then used to calculate the coefficient of variation.

The within-subject variability is Root MSE below. For example, for rbc it is 0.861472 (which is the square root of Residual MS = 0.742134798.

Similarly for serum, below.

```
.
. drop if OBS==1
(1397 observations deleted)

. set matsize 800

.
. anova rbcresult employeeid obs if obs<3

                           Number of obs =     704     R-squared     =  0.6208
                           Root MSE      = .861472     Adj R-squared =  0.2405

                  Source |  Partial SS    df       MS           F     Prob > F
              -----------+----------------------------------------------------
                   Model |  426.439902   352  1.21147699       1.63     0.0000
                         |
              employeeid |   426.16782   351  1.21415333       1.64     0.0000
                     obs |  .272081852     1  .272081852       0.37     0.5452
                         |
                Residual |  260.489314   351  .742134798
              -----------+----------------------------------------------------
                   Total |  686.929216   703   .97713971
```

Coefficient of variation calculation for rbc
Use only obs==1 (that is, the initial observation.

n=1747 mean = 5.718569 CV=0.861472/5.718569 = 15.1%

(The means comes from the earlier tables on page 2)

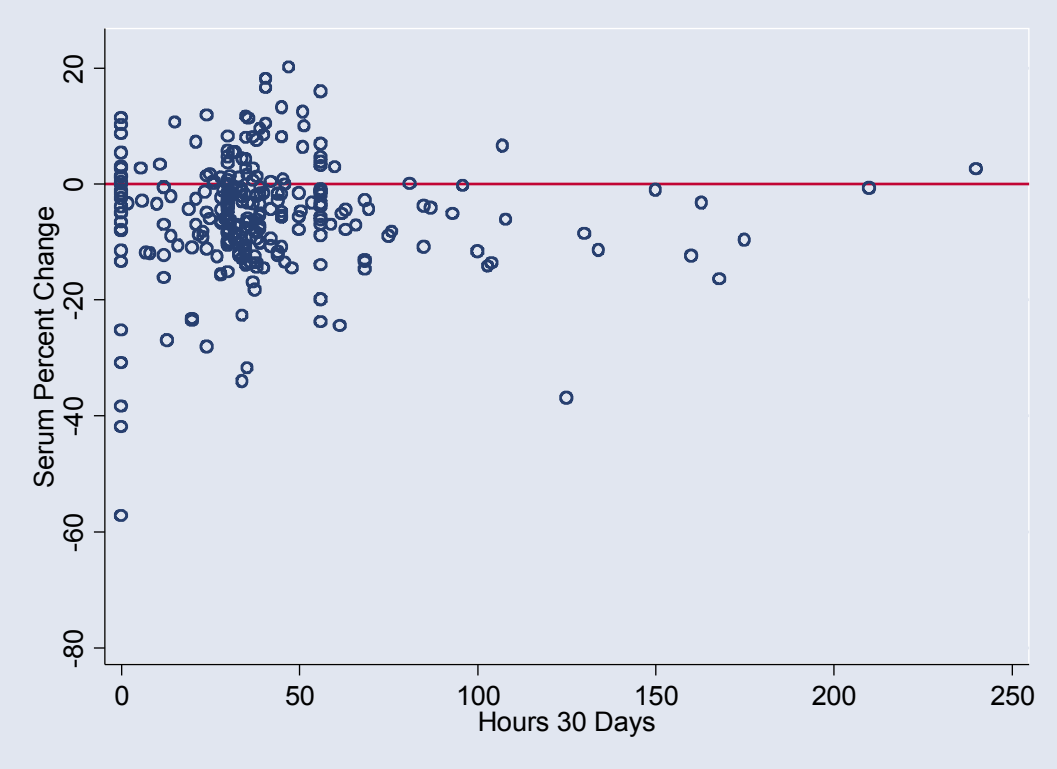
```
. anova serumresult employeeid obs if obs<3

                           Number of obs =     704     R-squared     =  0.9219
                           Root MSE      = .804903     Adj R-squared =  0.8436

                  Source |  Partial SS    df       MS           F     Prob > F
              -----------+----------------------------------------------------
                   Model |  2683.88929   352  7.62468547      11.77     0.0000
                         |
              employeeid |  2630.33532   351  7.49383283      11.57     0.0000
                     obs |  53.5539647     1  53.5539647      82.66     0.0000
                         |
                Residual |   227.40219   351  .647869488
              -----------+----------------------------------------------------
                   Total |  2911.29148   703  4.14123966
```

Coefficient of variation calculation for serum
Use only obs==1 (that is, the initial observation.

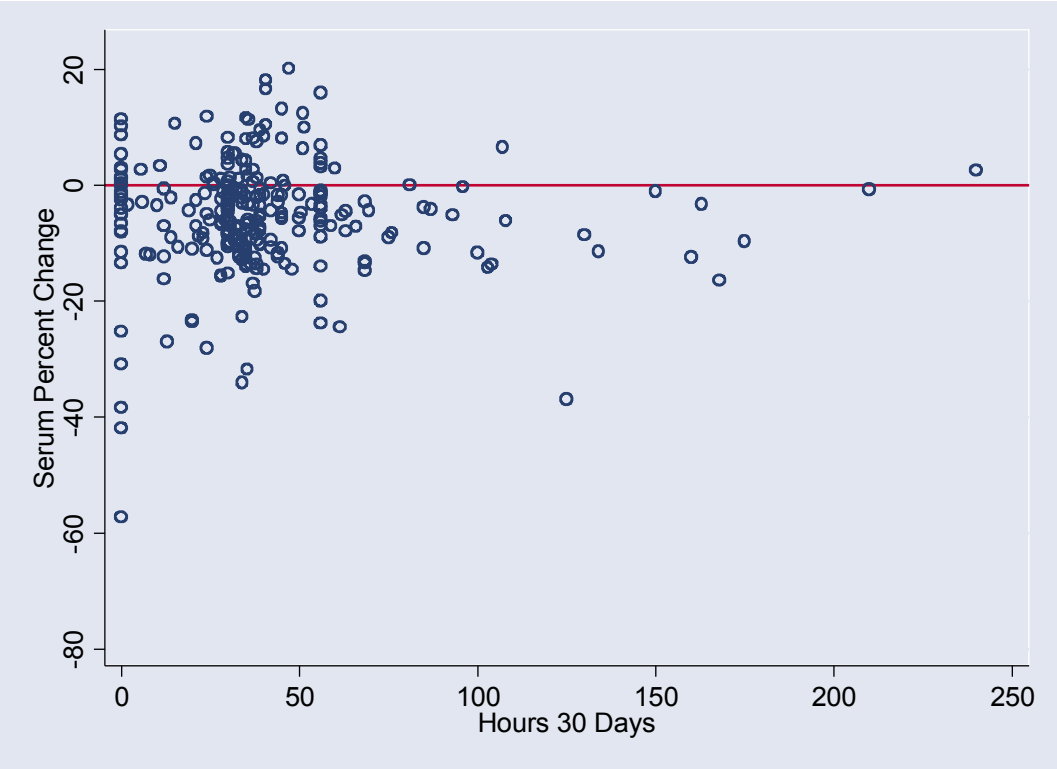
n=1749 mean = 11.80813 CV= 0.8404903/11.80813 = 7.1%

```
. corr rbcpercentchange serumpercentchange hours30days hourstotal
(obs=193)

             | rbcper~e serump~e hours3~s hourst~l
-------------+------------------------------------
rbcpercent~e |   1.0000
serumperce~e |   0.0238   1.0000
 hours30days |   0.1205   0.1251   1.0000
  hourstotal |   0.0977   0.0206   0.5610   1.0000


.
. regress rbcpercentchange hours30days

      Source |       SS       df       MS              Number of obs =     267
-------------+------------------------------           F(  1,   265) =    1.26
       Model |  457.181152     1  457.181152           Prob > F      =  0.2629
    Residual |  96235.6738   265  363.153486           R-squared     =  0.0047
-------------+------------------------------           Adj R-squared =  0.0010
       Total |   96692.855   266  363.506974           Root MSE      =  19.057

------------------------------------------------------------------------------
rbcpercent~e |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
 hours30days |   .0398068   .0354779     1.12   0.263    -.0300477    .1096613
       _cons |  -3.429536   1.845982    -1.86   0.064    -7.064193    .2051216
------------------------------------------------------------------------------

. regress serumpercentchange hours30days

      Source |       SS       df       MS              Number of obs =     267
-------------+------------------------------           F(  1,   265) =    0.01
       Model |  1.24421785     1  1.24421785           Prob > F      =  0.9088
    Residual |  25103.7329   265  94.7310675           R-squared     =  0.0000
-------------+------------------------------           Adj R-squared = -0.0037
       Total |  25104.9771   266  94.3796132           Root MSE      =   9.733
```

```
------------------------------------------------------------------------------
serumperce~e |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
 hours30days |   .0020766   .0181201     0.11   0.909     -.033601    .0377542
       _cons |  -5.589761   .9428194    -5.93   0.000    -7.446131   -3.733391
------------------------------------------------------------------------------

. regress rbcpercentchange hourstotal

      Source |       SS       df       MS              Number of obs =     230
-------------+------------------------------           F(  1,   228) =    0.65
       Model |  216.880737     1  216.880737           Prob > F      =  0.4220
    Residual |  76431.6363   228  335.226475           R-squared     =  0.0028
-------------+------------------------------           Adj R-squared = -0.0015
       Total |   76648.517   229  334.709681           Root MSE      =  18.309

------------------------------------------------------------------------------
rbcpercent~e |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  hourstotal |    .018098   .0225004     0.80   0.422    -.0262372    .0624333
       _cons |  -2.724983   1.988945    -1.37   0.172    -6.644046     1.19408
------------------------------------------------------------------------------

.
.
.
. regress serumpercentchange hourstotal

      Source |       SS       df       MS              Number of obs =     230
-------------+------------------------------           F(  1,   228) =    0.13
       Model |  11.1946236     1  11.1946236           Prob > F      =  0.7177
    Residual |  19472.3959   228  85.4052452           R-squared     =  0.0006
-------------+------------------------------           Adj R-squared = -0.0038
       Total |  19483.5905   229  85.0811814           Root MSE      =  9.2415

------------------------------------------------------------------------------
serumperce~e |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  hourstotal |   .0041117    .011357     0.36   0.718    -.0182663    .0264898
       _cons |  -6.066662   1.003912    -6.04   0.000    -8.044795    -4.08853
------------------------------------------------------------------------------


. twoway scatter rbcpercentchange hours30days, yline(0)
```

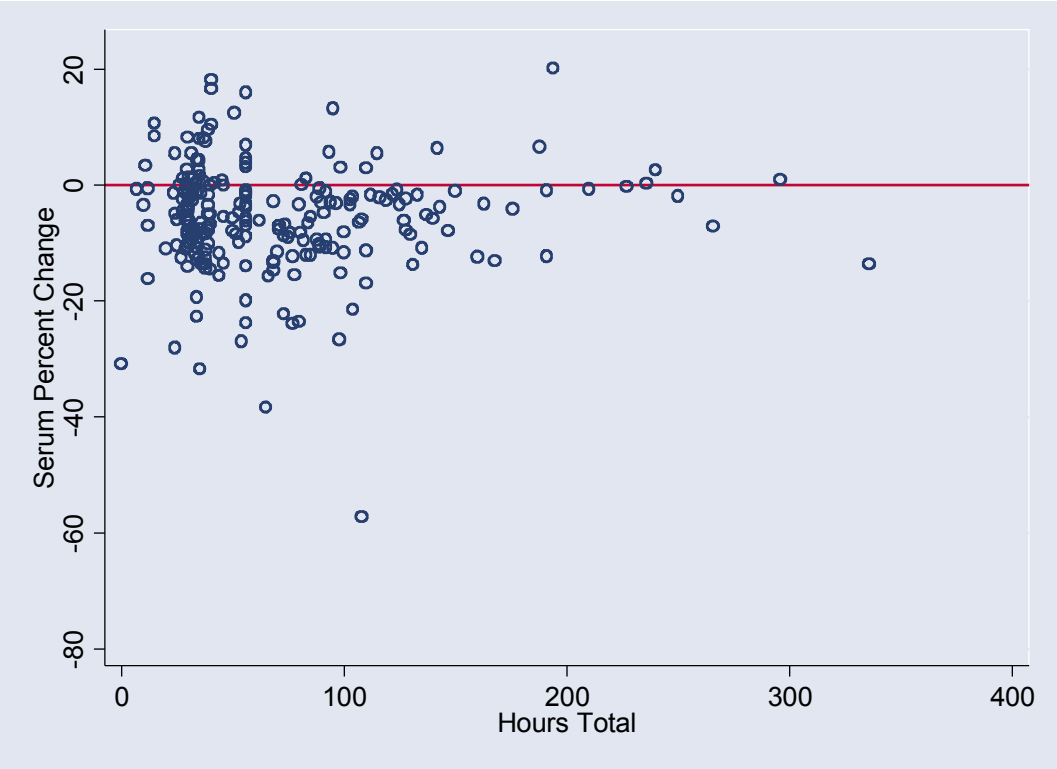

Serum Percent Change
20
0
-20
-40
-60
-80
0
50
100
150
200
250
Hours 30 Days

```
. twoway scatter serumpercentchange hours30days, yline(0)
```



.

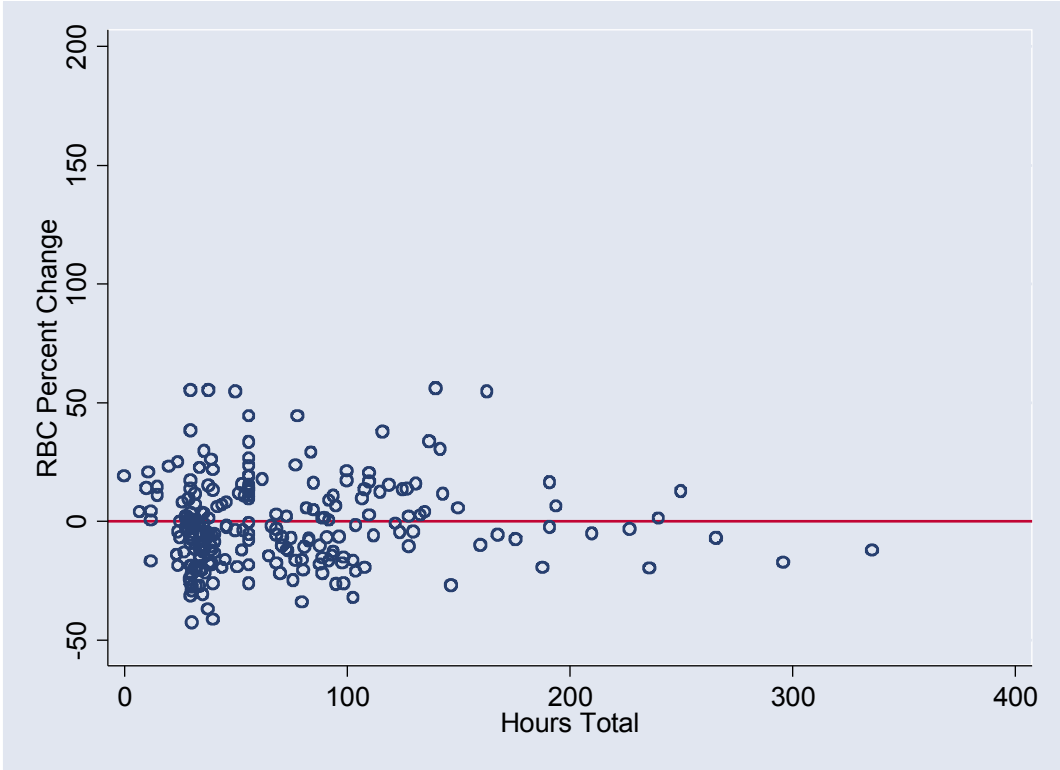
```
twoway scatter serumpercentchange hourstotal, yline(0)
```




```
. twoway scatter rbcpercentchange hourstotal, yline(0)
```

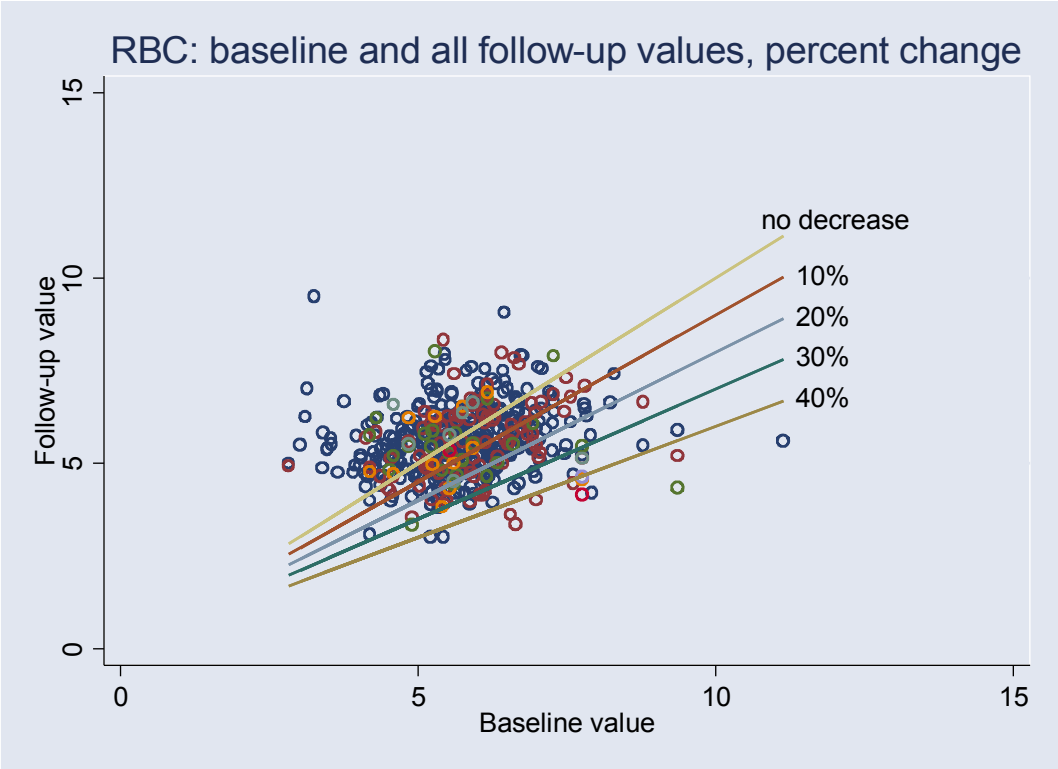
.

```
. keep employeeid rbcresult serumresult rbcpercentchange serumpercentchange obs
```

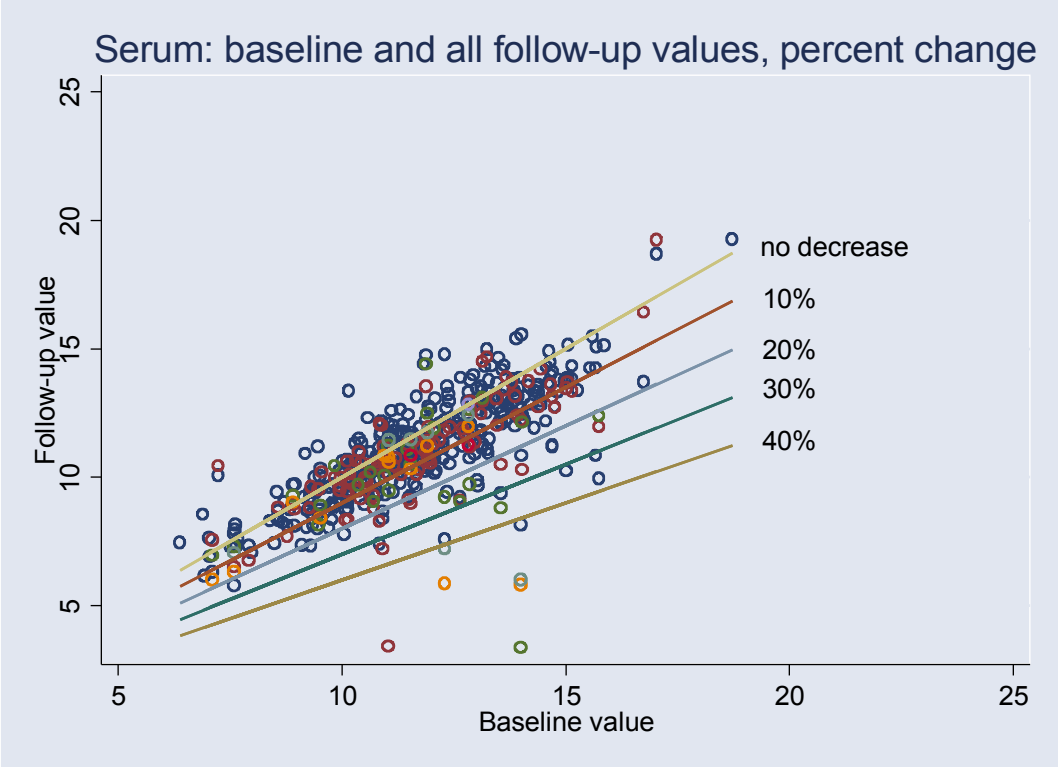



```
.
reshape wide rbcresult serumresult rbcpercentchange serumpercentchange,i(employeeid)
j(obs)
(note: j = 1 2 3 4 5 6 7 8)

Data                               long   ->   wide
-----------------------------------------------------------------------------
Number of obs.                      855   ->     352
Number of variables                   6   ->      33
j variable (8 values)               obs   ->   (dropped)
xij variables:
                             rbcresult   ->   rbcresult1 rbcresult2 ... rbcresult8
                           serumresult   ->   serumresult1 serumresult2 ... serumresult8
                      rbcpercentchange   ->   rbcpercentchange1 rbcpercentchange2 ...
rbcpercentchange8
                     serumpercentchange   ->   serumpercentchange1 serumpercentchange2
... serumpercentchange8
-----------------------------------------------------------------------------

.
. **************graph for rbc***************
. gen rt9y1=0.9*rbcresult1

. gen rt8y1=0.8*rbcresult1

. gen rt7y1=0.7*rbcresult1

. gen rt6y1=0.6*rbcresult1

.
. twoway (scatter rbcresult2 rbcresult1) /*
> */(scatter rbcresult3 rbcresult1) (scatter rbcresult4 rbcresult1) (scatter rbcresult5
rbcresult1)/*
> */(scatter rbcresult6 rbcresult1) (scatter rbcresult7 rbcresult1) (scatter rbcresult8
rbcresult1)/*
> */(line rbcresult1 rbcresult1) (line rt9y1 rbcresult1 )(line rt8y1 rbcresult1 )/*
> */(line rt7y1 rbcresult1 )  (line  rt6y1 rbcresult1), /*
```

```
> */legend(off) xlabel(0 5 10 15 ) ylabel(0 5 10 15) xtitle (Baseline value)
ytitle(Follow-up value)/*
> */title("RBC: baseline and all follow-up values, percent change")/*
> */text(11.6 12 "no decrease") text( 10.1 11.8  "10%")  text(9 11.8 "20%") text(7.9 11.8
"30%") text(6.8 11.8 "40%")
```




```
. ********************************8
.
.
.
. ***********graph for serum**********
.
. gen pt9y1=0.9*serumresult1

. gen pt8y1=0.8*serumresult1

. gen pt7y1=0.7*serumresult1

. gen pt6y1=0.6*serumresult1

.
. twoway (scatter serumresult2 serumresult1) /*
> */(scatter serumresult3 serumresult1) (scatter serumresult4 serumresult1) (scatter
serumresult5 serumresult1)/*
> */(scatter serumresult6 serumresult1) (scatter serumresult7 serumresult1) (scatter
serumresult8 serumresult1)/*
> */(line serumresult1 serumresult1) (line pt9y1 serumresult1 )(line pt8y1 serumresult1 )
/*
> */(line pt7y1 serumresult1 )  (line  pt6y1 serumresult1), /*
> */legend(off) xlabel(0 5 10 15 20) ylabel(0 5 10 15 20) xtitle (Baseline value)
ytitle(Follow-up value)/*
> */title("Serum: baseline and all follow-up values, percent change")/*
> */text(17.5 17.5 "no decrease") text( 15.3 17.7  "10%")  text(13.6 17.7 "20%")
text(11.9 17.7 "30%") text(10.2 17.7 "40%")
```




```
. ********************************8
.
. gen rbcdel1=rbcresult1-rbcresult2

. gen serumdel1=serumresult1-serumresult2

. sum rbcresult1 rbcresult2 rbcdel1

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
  rbcresult1 |       352     5.68375    1.036924       2.83      11.14
  rbcresult2 |       352    5.644432    .9386571        3.6       9.49
     rbcdel1 |       352    .0393182    1.218306      -6.23       5.55

. sum serumresult1 serumresult2 serumdel1

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
serumresult1 |       352    11.70429    2.004094       6.38      18.72
serumresult2 |       352    11.15267    2.031086       6.14      19.25
   serumdel1 |       352    .5516193    1.138305      -4.84   4.790001

. sum

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
  employeeid |       352    996.9148    1243.492         12       9081
  rbcresult1 |       352     5.68375    1.036924       2.83      11.14
serumresult1 |       352    11.70429    2.004094       6.38      18.72
rbcpercent~1 |         1       14.79           .      14.79      14.79
serumperce~1 |         1        5.35           .       5.35       5.35
-------------+--------------------------------------------------------
  rbcresult2 |       352    5.644432    .9386571        3.6       9.49
serumresult2 |       352    11.15267    2.031086       6.14      19.25
rbcpercent~2 |       335    1.820444    24.64385     -49.82      191.1
serumperce~2 |       334   -4.226124    8.804776     -28.16      23.91
  rbcresult3 |       103    5.547087    1.011648       3.01       7.94
-------------+--------------------------------------------------------
```

serumresult3	103	10.81146	2.255855	3.36	18.67
rbcpercent~3	102	-5.574772	20.66742	-53.79	55.83
serumperce~3	102	-7.199216	12.52492	-76.01713	21.91
rbcresult4	26	5.500769	1.08383	3.33	8.01
serumresult4	26	9.76	2.242361	3.42	13.53
rbcpercent~4	26	-1.690333	24.63636	-44.61	51.42
serumperce~4	26	-14.55337	16.9927	-69.02174	2.66
rbcresult5	12	5.543333	.7168027	4.51	6.63
serumresult5	12	9.38	2.131291	5.99	12.39
rbcpercent~5	12	2.517231	20.28849	-34.1	43.14
serumperce~5	12	-11.20864	18.74827	-57.24	6.188467
rbcresult6	7	5.35	.4827008	4.56	5.9
serumresult6	7	10.11571	2.973583	5.77	12.48
rbcpercent~6	7	-3.183419	22.28642	-41.31274	23.53
serumperce~6	7	-12.16579	22.62447	-58.52962	4.697987
rbcresult7	2	5.555	.1343503	5.46	5.65
serumresult7	2	10.795	2.580939	8.97	12.62
rbcpercent~7	2	-13.87	22.41528	-29.72	1.98
serumperce~7	2	-10.315	16.90692	-22.27	1.64
rbcresult8	1	4.15	.	4.15	4.15
serumresult8	1	11.25	.	11.25	11.25
rbcpercent~8	1	-46.58	.	-46.58	-46.58
serumperce~8	1	-12.31	.	-12.31	-12.31
rt9y1	352	5.115375	.9332314	2.547	10.026
rt8y1	352	4.547	.8295391	2.264	8.912001
rt7y1	352	3.978625	.7258467	1.981	7.798
rt6y1	352	3.41025	.6221543	1.698	6.684
pt9y1	352	10.53386	1.803685	5.742	16.848
pt8y1	352	9.363432	1.603275	5.104	14.976
pt7y1	352	8.193003	1.402866	4.466	13.104
pt6y1	352	7.022574	1.202456	3.828	11.232
rbcdel1	352	.0393182	1.218306	-6.23	5.55
serumdel1	352	.5516193	1.138305	-4.84	4.790001

.