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## The Assessment of the Degree of Concordance Between the Observed Values and the Predicted Values of a Mixed-Effect Model Using “Method of Comparison” Techniques

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# The Assessment of the Degree of Concordance Between the Observed Values and the Predicted Values of a Mixed-Effect Model Using “Method of Comparison” Techniques

William F. McCarthy and Nan Guo

## **Abstract**

In this paper, we present a methodology for determining the degree of concordance between observed and model-based predicted values of a mixed-effect model. In particular, we will compare the degree to which observed and model-based predicted values agree by using ‘method of comparison’ techniques. We will also present the results of the concordance correlation coefficient (CCC).

## Introduction

In linear mixed models, few diagnostic tools are available for assessing adequacy of the model. There are a number of statistics that are often used and available in the SAS System:

AIC	$-2l + 2d$	Akaike (1974)
AICC	$-2l + 2d \frac{n}{n-d-1}$	Hurvich and Tsai (1989)
		Burnham and Anderson (1998)
HQIC	$-2l + 2d \log n$	Hannan and Quinn (1979)
BIC	$-2l + d \log n$	Schwarz (1978)
CAIC	$-2l + d(\log n + 1)$	Bozdogan (1987)

Here  $l$  denotes the maximum value of the (possibly restricted) log likelihood,  $d$  the dimension of the model, and  $n$  the number of observations. In Version 6 of SAS/STAT software,  $n$  equals the number of valid observations for maximum likelihood estimation and  $n-p$  for restricted maximum likelihood estimation, where  $p$  equals the rank of  $X$ . In later versions,  $n$  equals the number of effective subjects as displayed in the "Dimensions" table, unless this value equals 1, in which case  $n$  equals the number of levels of the first RANDOM effect you specify. If the number of effective subjects equals 1 and you have no RANDOM statements, then  $n$  reverts to the Version 6 values. For AICC (a finite-sample corrected version of AIC),  $n$  equals the Version 6 values of  $n$ , unless this number is less than  $d+2$ , in which case it equals  $d+2$ .

For restricted likelihood estimation,  $d$  equals  $q$  the effective number of estimated covariance parameters. In Version 6, when a parameter estimate lies on a boundary constraint, then it is still included in the calculation of  $d$ , but in later versions it is not. The most common example of this behavior is when a variance component is estimated to equal zero. For maximum likelihood estimation,  $d$  equals  $q+p$ .

These statistics can be useful when comparing the fit of several models to the same data. They are information criteria that are in "smaller-is-better" form. However, the problem with these statistics for assessing goodness of fit is that they may not be intuitively interpretable in that they do not have well defined endpoints corresponding to a perfect fit or a complete lack of fit. That is, given a linear mixed model, these statistics do not provide us with a sense of how good the model (on some scale) is and how much improvement might be needed. For example, in traditional ANOVA an  $r^2$  of 0.8 can be interpreted as "80% of the variation in the dependent variable can be explained by the independent variable(s)".

A goodness-of-fit statistic called the concordance correlation coefficient (CCC) was introduced by Lin in 1989. The concordance correlation coefficient (Lin, 1989) evaluates the degree to which pairs of observations fall on the  $45^\circ$  line through the origin. Vonesh et al. (1996) proposed to use the CCC to compare the degree to which observed and expected values agree for a large class of models that include the mixed-effect model. The CCC is very similar to 'methods of comparison' such as the Bland Altman plot (as well as a 95% confidence interval of the mean difference between the observed and expected values; Bland and Altman, 1983;1986;1999), Deming regression (Combleet & Gochman, 1979), Passing-Bablok regression Passing & Bablok (1983), and Mountain plots (Krouwer & Monti, 1995). "The CCC measures agreement between two methods or time points by measuring the variation of their linear relationship from the  $45^\circ$  line through the origin. Therefore, this coefficient is not only measuring how far each observation deviates from the line fit to the data (precision), but also how far this line deviates from the  $45^\circ$  line through the origin (accuracy)", King T.S. et al., 2007.

Methods for comparing the degree of concordance between observed and model predictive values have been proposed by Gönen and Heller (2005) and Harrell et al (1982, 1984). These concordance indices are probabilities on  $[0,1]$  with 1 representing a model that has perfect discrimination (perfect 'predictive validity') and 0.5 indicating that a coin toss would be more predictive than the model under assessment. Comparing the degree of concordance between observed and model predictive values of a mixed-effect

model has been done in an informal manner by Ross et al (1994) by comparing the actual mean value with the model-based predicted value. This comparison was done qualitatively; no formal concordance assessment was done. In this paper, we present a methodology for determining the degree of concordance between observed and model-based predictive values of a mixed-effect model. In particular, we will compare the degree to which observed and model predicted values agree in a similar manner as proposed in the 'method of comparison' approaches. We will also present the results of the concordance correlation coefficient (CCC).

### **Method of Comparison**

Altman and Bland (1983;1986;1999) proposed an approach that we will use for analyzing observed and predicted data (the Bland Altman Plot). In order to assess the agreement of observed and predicted data graphically, the difference between the two values (observed and predicted) are plotted against the mean of the two values of the methods for each subject. Limits of agreement, defined as twice the standard deviation of the difference between the observed and predicted values, are calculated and plotted in the figure. If we suppose that these differences follow a normal distribution, 95% of the differences will lie between the limits of agreement. If the differences are Normally distributed (Gaussian), 95% of differences will lie between the limits of agreement (or, more precisely, between mean difference –

$2\text{standard deviation } [\bar{d} - 2s]$  and mean difference+ $2\text{standard deviation } [\bar{d} + 2s]$ ). Such differences are likely to follow a Normal distribution because we have removed a lot of the variation between subjects and are left with the measurement error. The values themselves do not have to follow a Normal distribution, and often they will not. We can check the distribution of the differences by drawing a histogram. If this is skewed or has very long tails the assumption of Normality may not be valid. We can also perform a Test of Normality. From this type of plot, it is easy to see if there is any tendency for the variation to change with the magnitude of the values. If the differences are symmetrical around zero, then there is no systematic bias. If the differences fall within the limits of agreement and the limits of agreement are considered to be clinically acceptable in terms of agreement, then one can say the observed and predicted values are in some sense comparable. If there is no relationship between the differences and the averages, the agreement between the observed and predicted values may be summarized using the means and standard deviations of the observed and predicted values.

Deming regression (Combleet & Gochman, 1979) is a method of linear regression that finds a line of best fit for a set of related data (observed and predicted values). It differs from simple linear regression in that it accounts for error in both the x and the y-axis. The line of regression (or line of best fit) must begin where your x and y axis meet (zero). If both sets of data (observed and predicted) contained error Deming regression would be more appropriate than linear regression.

Passing & Bablok (1983) have described a linear regression procedure with no special assumptions regarding the distribution of the samples and the measurement errors. The result does not depend on the assignment of the methods (or instruments) to X and Y. The slope B and intercept A are calculated with their 95% confidence interval. These confidence intervals are used to determine whether there is only a chance difference between B and 1 and between A and 0.

A Mountain Plot (folded empirical cumulative distribution plot) is created by computing a percentile for each ranked difference between the predicted and the observed value. To get a folded plot, the following transformation is performed for all percentiles above 50: percentile = 100 - percentile. These percentiles are then plotted against the differences between the predicted and observed values (Krouwer & Monti, 1995). The mountain plot is a useful complementary plot to the Bland & Altman plot. In particular, the mountain plot offers the following advantages: It is easier to find the central 95% of the data, even when the data are not Normally distributed and Different distributions can be compared more easily.

### **Example**

We will look at a mixed-effect model, using SAS 9.1.3 and compare the observed value of a clinical measure of interest to the predicted value generated by the mixed-effect model. The 'method of comparison' approaches mentioned earlier will be used to assess the degree of concordance of a mixed-

effect model. Statistical analyses for method comparison were performed using MedCalc for Windows, version 9.3.2.0 (MedCalc Software, Mariakerke, Belgium).

Creating the Mixed-effect Model and Resulting Predicted Values:

The entire data set used in this model can be found in Appendix A.

```
/* McCarthy Example of how to assess the degree of concordance of a linear
mixed effects model

using Sample 474: Longitudinal example using PROC MIXED found at

http://support.sas.com/ctx/samples/index.jsp?sid=474&tab=code

*/
data bp;
  input clinic$ stratum trt complier sbpb1 sbp3 sbp6 sbp9;
  person = _n_;
  array bp{3} sbp3 sbp6 sbp9;
  do i = 1 to 3;;
    visit = 3*i;
    visitlin = visit;
    sbp = bp{i};
    output;
  end;
  drop i ;*sbp3 sbp6 sbp9;
  datalines;
A 1 2 1 144.0 113 117 122
A 1 1 1 133.0 116 114 125
A 2 1 1 136.0 112 105 113
A 2 2 1 127.5 122 111 122
.
.
.
D 2 2 1 132.5 142 128 127
D 2 1 1 139.5 131 129 117
D 2 2 1 152.5 145 148 137
D 1 2 0 118.5 108 123 136
D 2 1 0 143.5 128 120 111
run;
```

```
/*---Model 6 with predicted values---*/
proc mixed data=bp;
  class trt visit complier clinic stratum person;
  model sbp = sbpb1 trt
    visit trt*visit
    complier trt*complier
    clinic trt*clinic
    stratum trt*stratum / outp=p;
  repeated visit / type=cs sub=person group=trt;
  id trt visit clinic person;
run;

proc transpose data=p out=perone(drop=_LABEL_ _NAME_) prefix=p;
  by person;
```

```

id visit;
/* id vstno;*/
var pred;
run;

proc sort data=bp
    out=uniq
        nodupkey;
    by person sbp3 sbp6 sbp9;
run;

data final;
merge uniq (IN=In_one keep=person sbp3 sbp6 sbp9 rename=(sbp3=o3 sbp6=o6
sbp9=o9))
    perone (IN=In_two);
by person;
run;

proc contents data=final;
run;

proc print;
run;

```

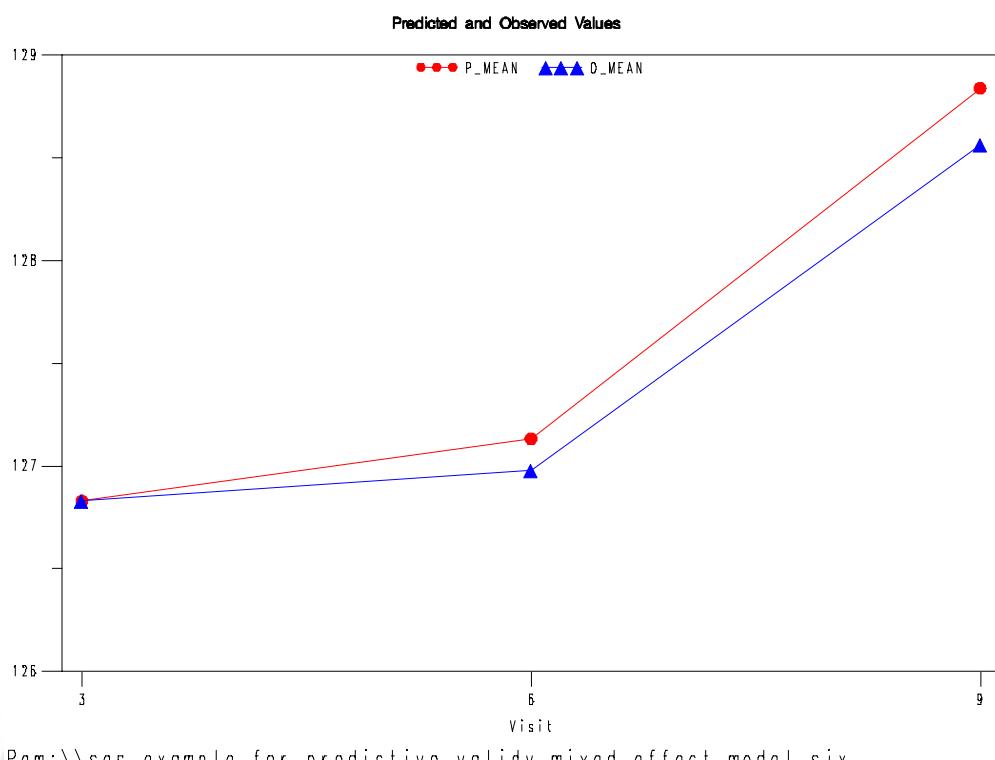
The resulting SAS output and SAS dataset for the degree of concordance assessment can be found in Appendix B. Below is a partial representation of the SAS data set to be used for the degree of concordance assessment. The observed values at visits 3, 6, and 9 are denoted o3, o6, and o9. The predicted values at visits 3, 6, and 9 are denoted p3, p6, and p9.

Obs	o3	o6	o9	person	p3	p6	p9
1	113	117	122	1	127.754	127.686	129.177
2	116	114	125	2	117.228	118.077	119.911
3	112	105	113	3	117.257	118.106	119.941
4	122	111	122	4	119.844	119.776	121.267
5	108	106	106	5	109.329	110.178	112.012
6	129	137	139	6	137.783	137.715	139.206
7	130	111	136	7	124.063	124.912	126.746
8	117	116	113	8	129.413	129.345	130.836
9	117	121	124	9	116.290	116.222	117.713
10	159	127	133	10	139.423	139.355	140.846
	.	.	.				

### Assessment of the Degree of Concordance:

Below is the typical graphic one sees when comparing the mean observed values to the mean predicted values. This graphic seems to indicate that the agreement between the observed and predicted values is reasonably close. We will now further assess the agreement between the observed and predicted values using the “method of comparison” techniques.

Figure 1.

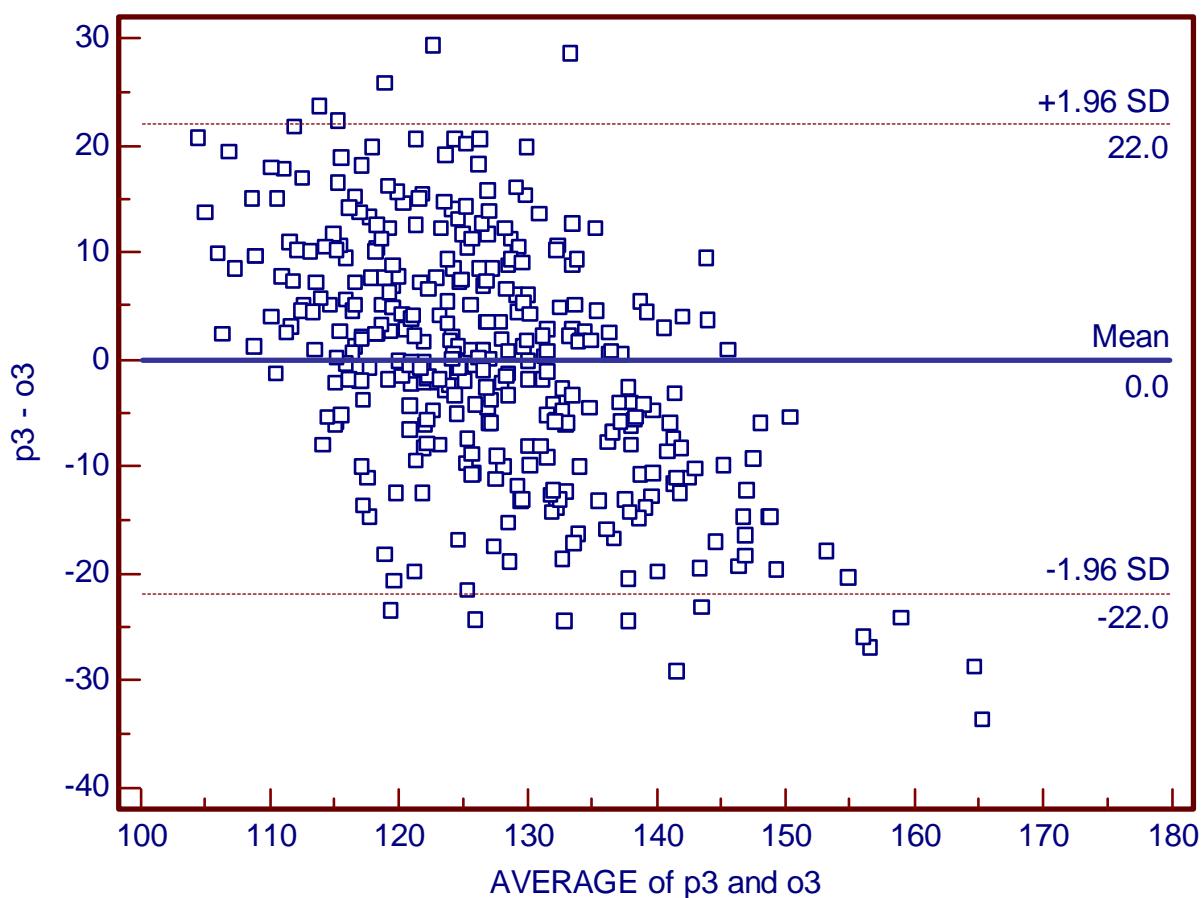


For each visit, we performed a ‘method of comparison’ analysis to assess the degree of concordance between observed and predicted values of the mixed-effect model.

- Bland Altman Plot

Visit 3

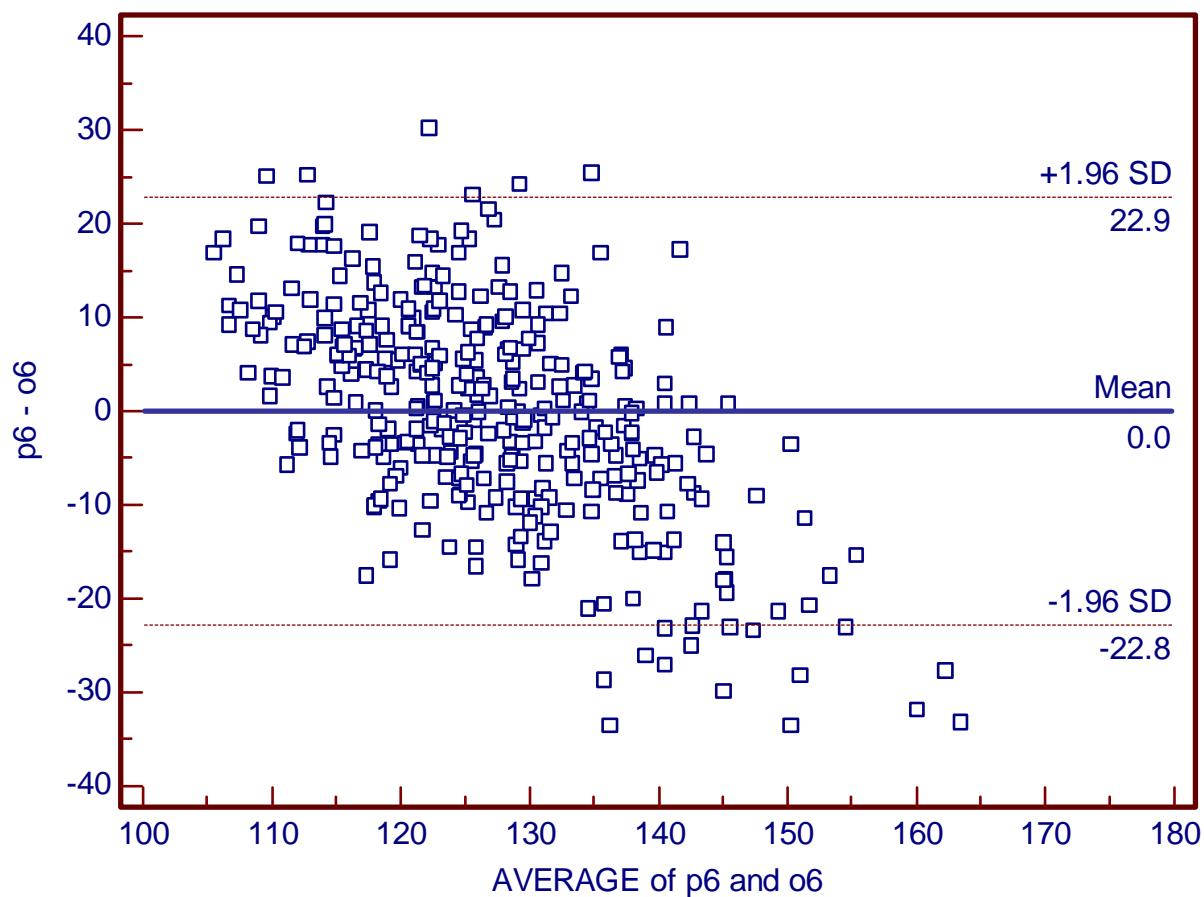
Figure 2.



- Bland Altman Plot

Visit 6

Figure 3.



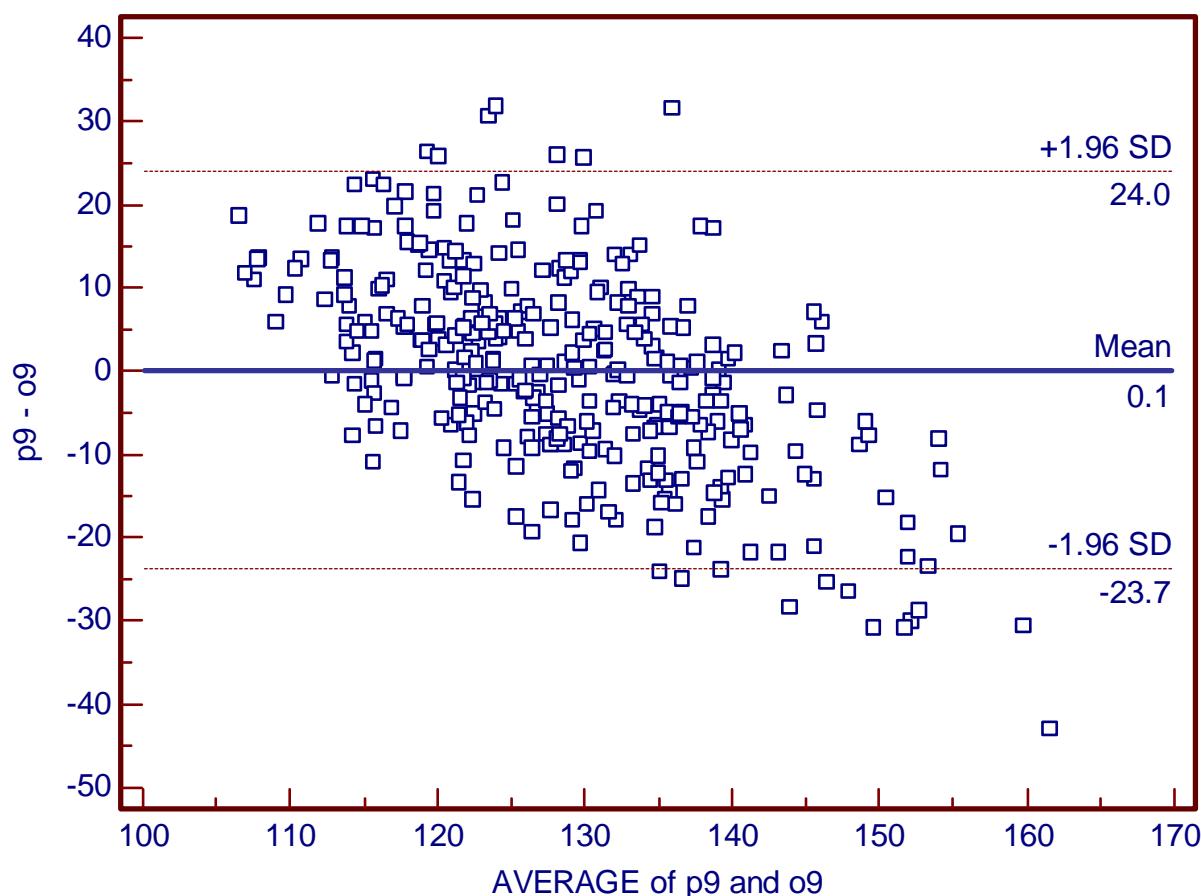
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- Bland Altman Plot

Visit 9

Figure 4.



- Deming regression

Visit 3

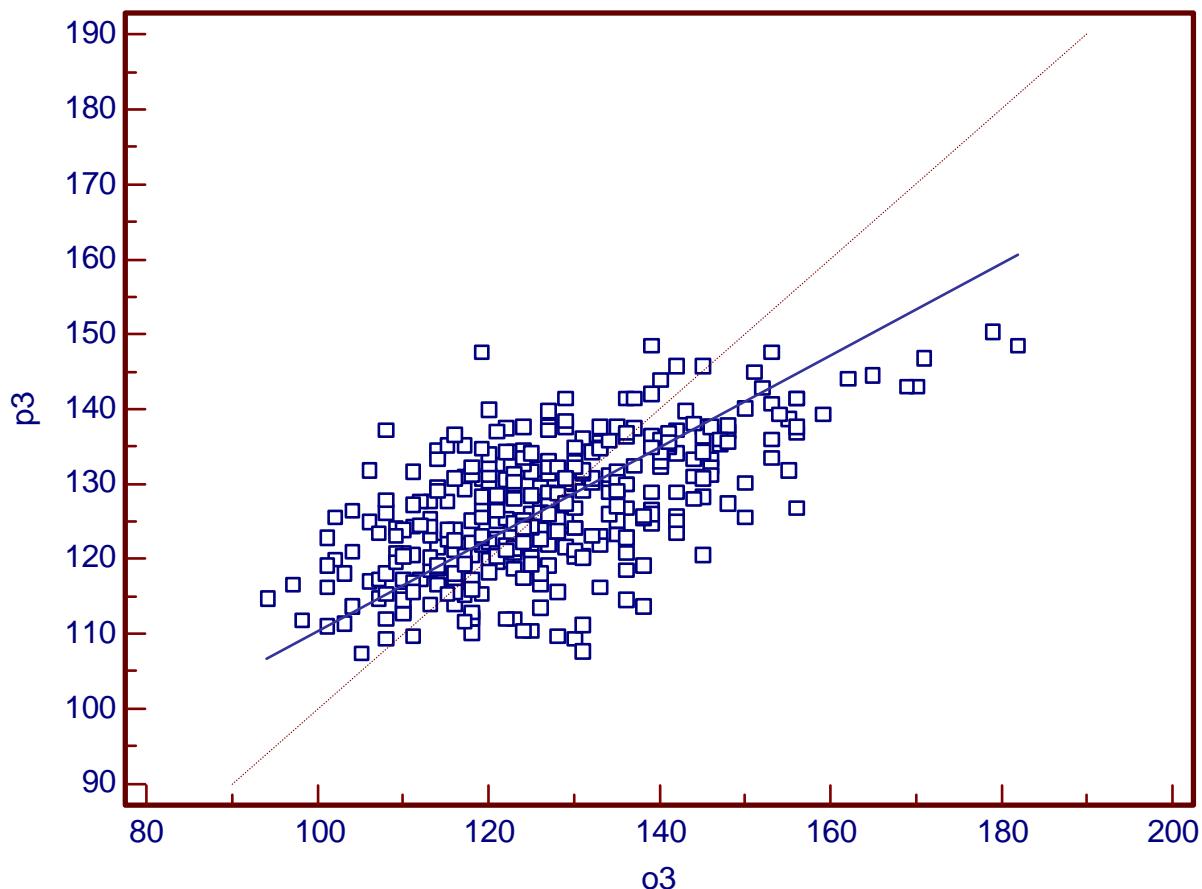


Figure 5. Regression graphic.



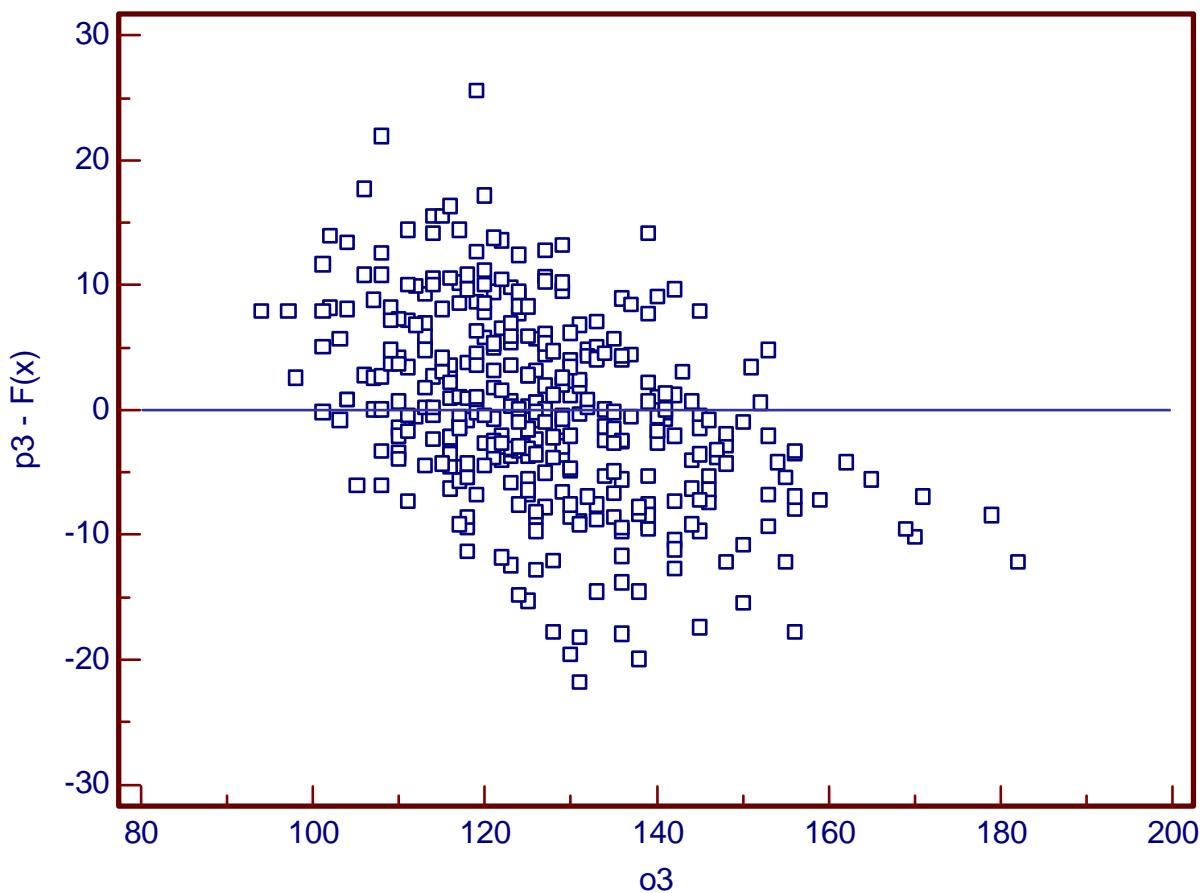


Figure 6. Residuals.

Table 1.

Deming regression		
Method X	<b>o3</b>	
Method Y	<b>p3</b>	
Method	Mean	Coefficient of Variation (%)
X	<b>126.8296</b>	<b>11.30</b>
Y	<b>126.8296</b>	<b>6.91</b>
Sample size		<b>358</b>
Variance ratio		<b>2.6719</b>
<i>Regression Equation</i>		
<b>y = 49.2676 + 0.6115 x</b>		
Parameter	Coefficient	Std.Error
Intercept	<b>49.2676</b>	<b>4.9942</b>
Slope	<b>0.6115</b>	<b>0.03936</b>
		95%CI
		<b>39.4458 to 59.0894</b>
		<b>0.5341 to 0.6890</b>

- Deming regression

Visit 6

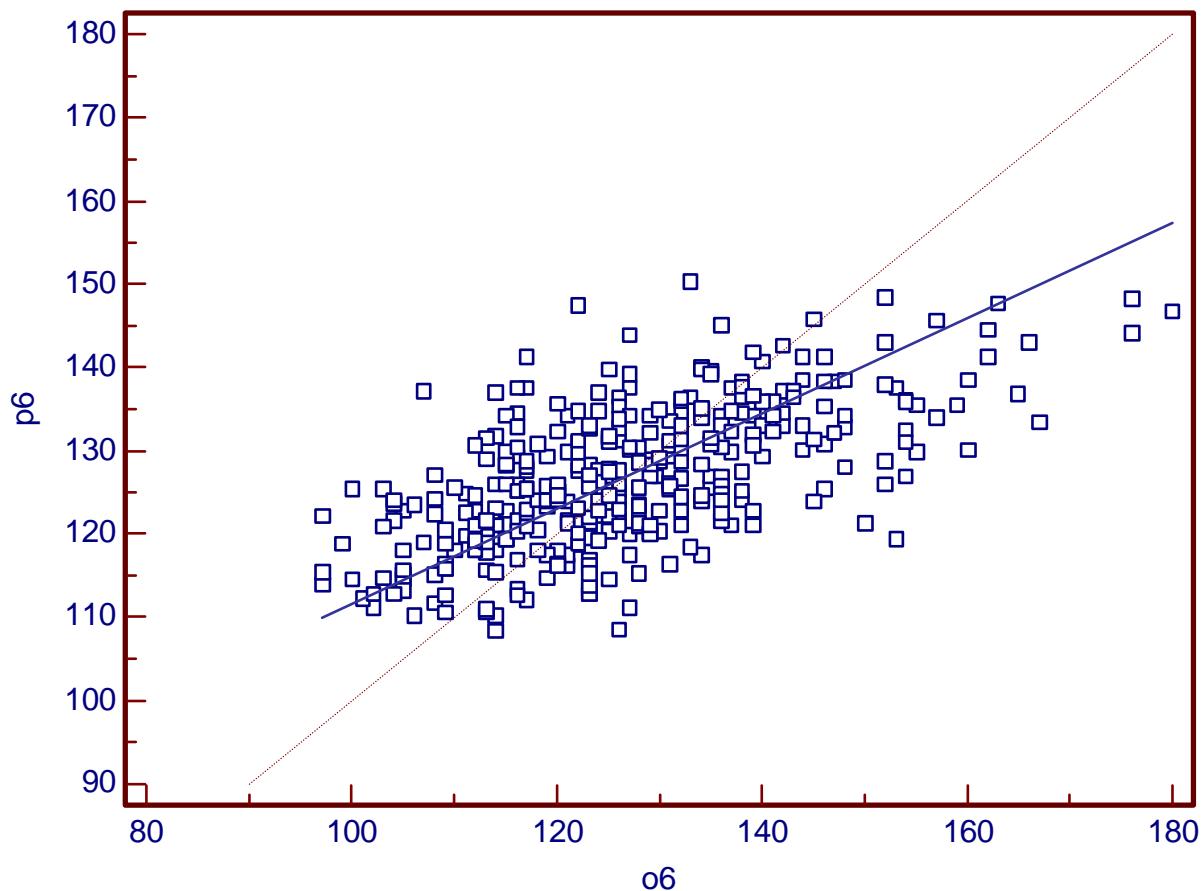


Figure 7. Regression graphic.



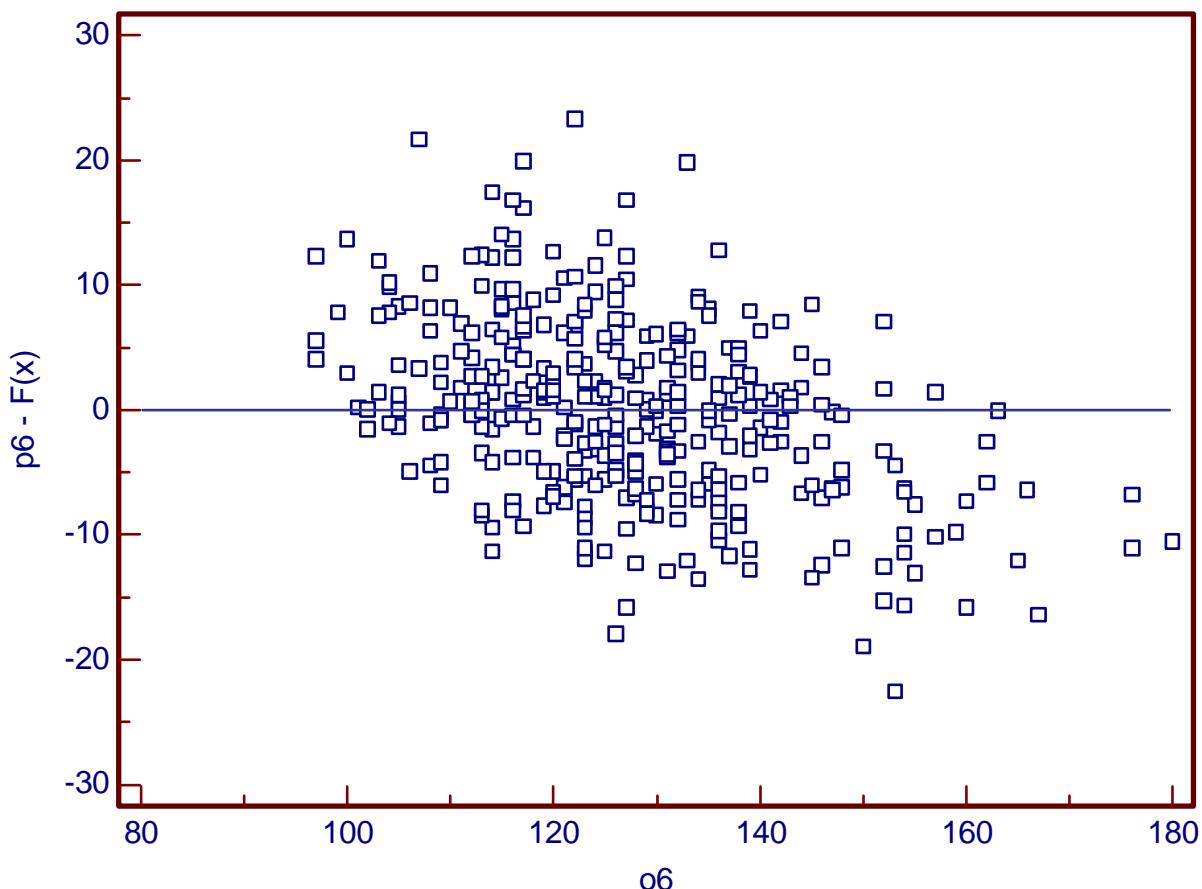


Figure 8. Residuals.

Table 2.

Deming regression				
Method X	<b>o6</b>			
Method Y	<b>p6</b>			
Method	Mean	Coefficient of Variation (%)		
X	<b>126.9773</b>	11.71		
Y	<b>127.0215</b>	6.77		
Sample size	<b>352</b>			
Variance ratio	<b>2.9862</b>			
<i>Regression Equation</i>				
<b>y = 54.3557 + 0.5723 x</b>				
Parameter	Coefficient	Std.Error		
Intercept	<b>54.3557</b>	<b>4.8637</b>		
Slope	<b>0.5723</b>	<b>0.03881</b>		
	<b>44.7900 to 63.9213</b>			
	<b>0.4959 to 0.6486</b>			

- Deming regression

Visit 9

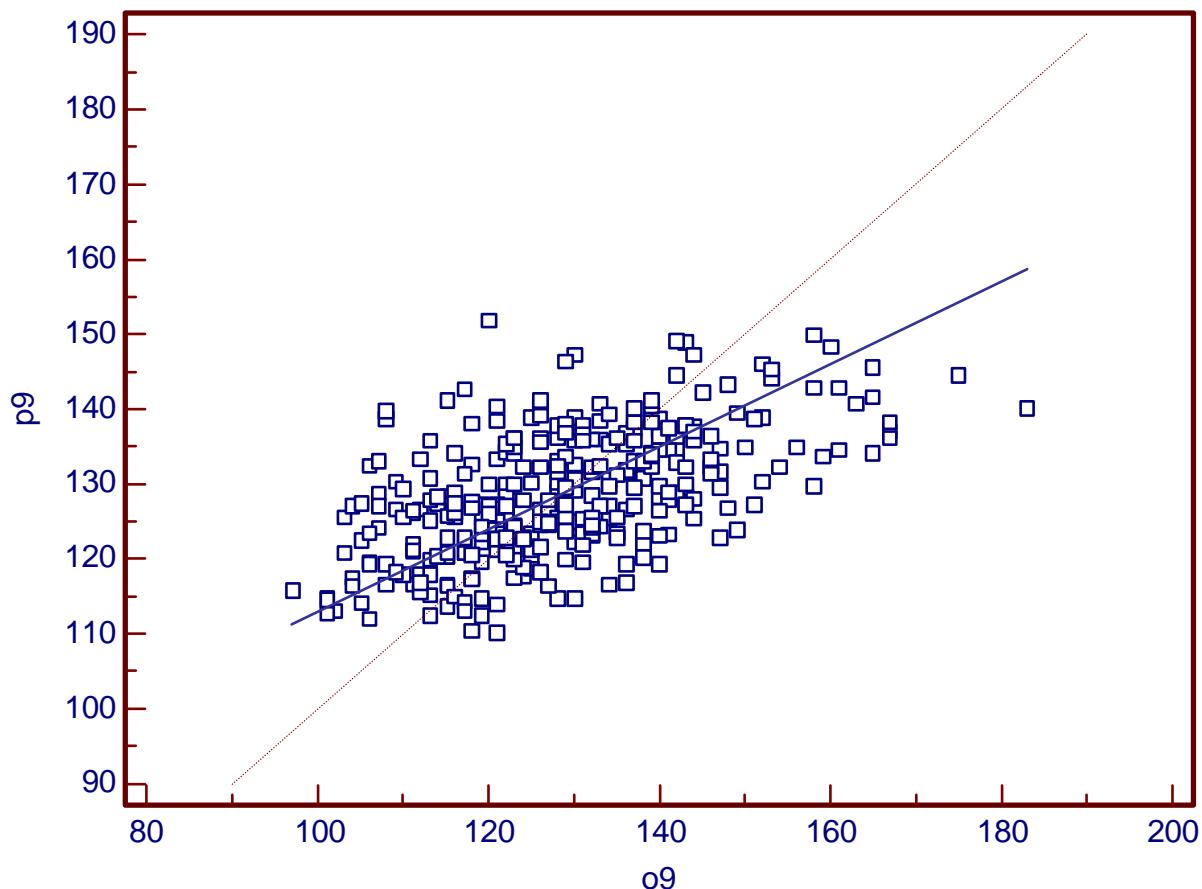


Figure 9. Regression graphic.



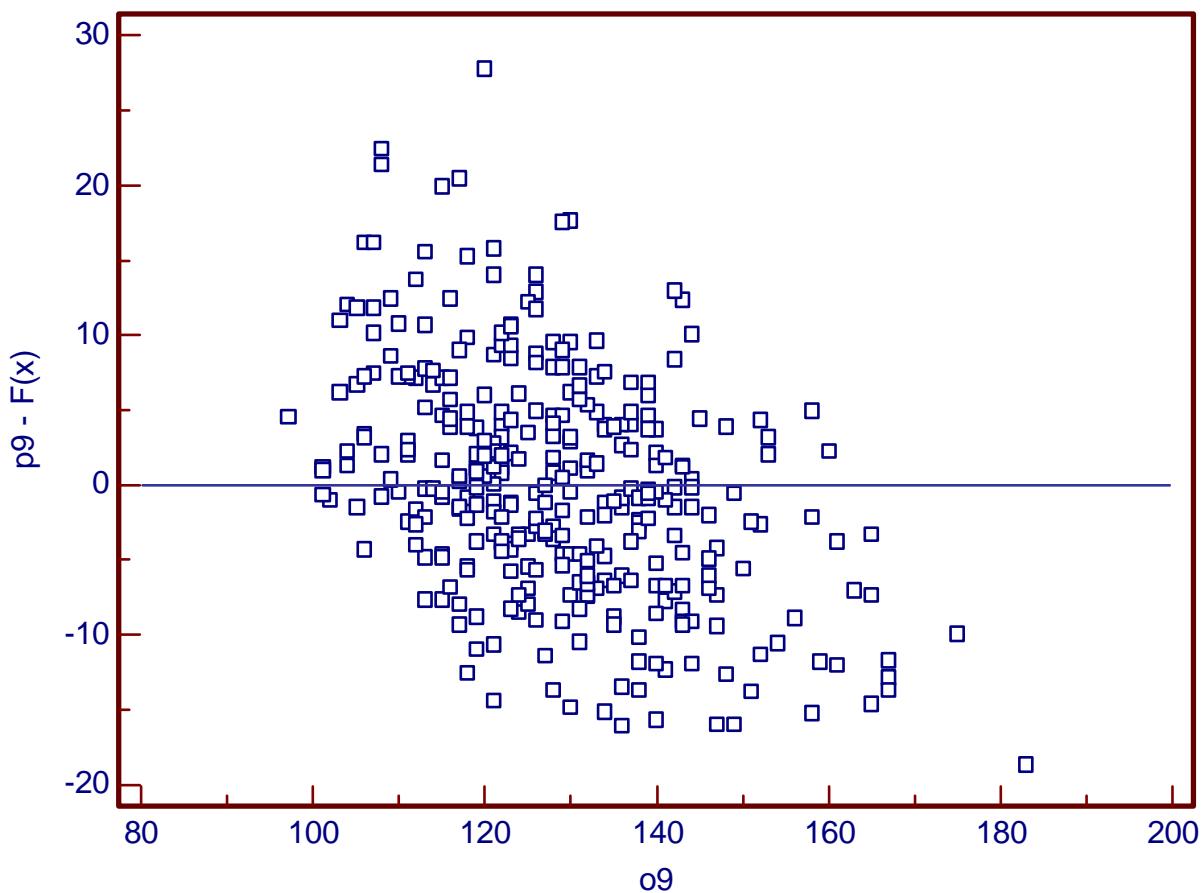


Figure 10. Residuals.

Table 3.

Deming regression				
Method X	o9			
Method Y	p9			
Method	Mean	Coefficient of Variation (%)		
X	128.5659	11.40		
Y	128.7128	6.81		
Sample size	334			
Variance ratio	2.7951			
<i>Regression Equation</i>				
$y = 57.6726 + 0.5526 \times x$				
Parameter	Coefficient	Std.Error		
Intercept	57.6726	5.8970		
Slope	0.5526	0.04648		
	95%CI			
	46.0726 to 69.2726			
	0.4611 to 0.6440			

- Passing & Bablok regression

Visit 3

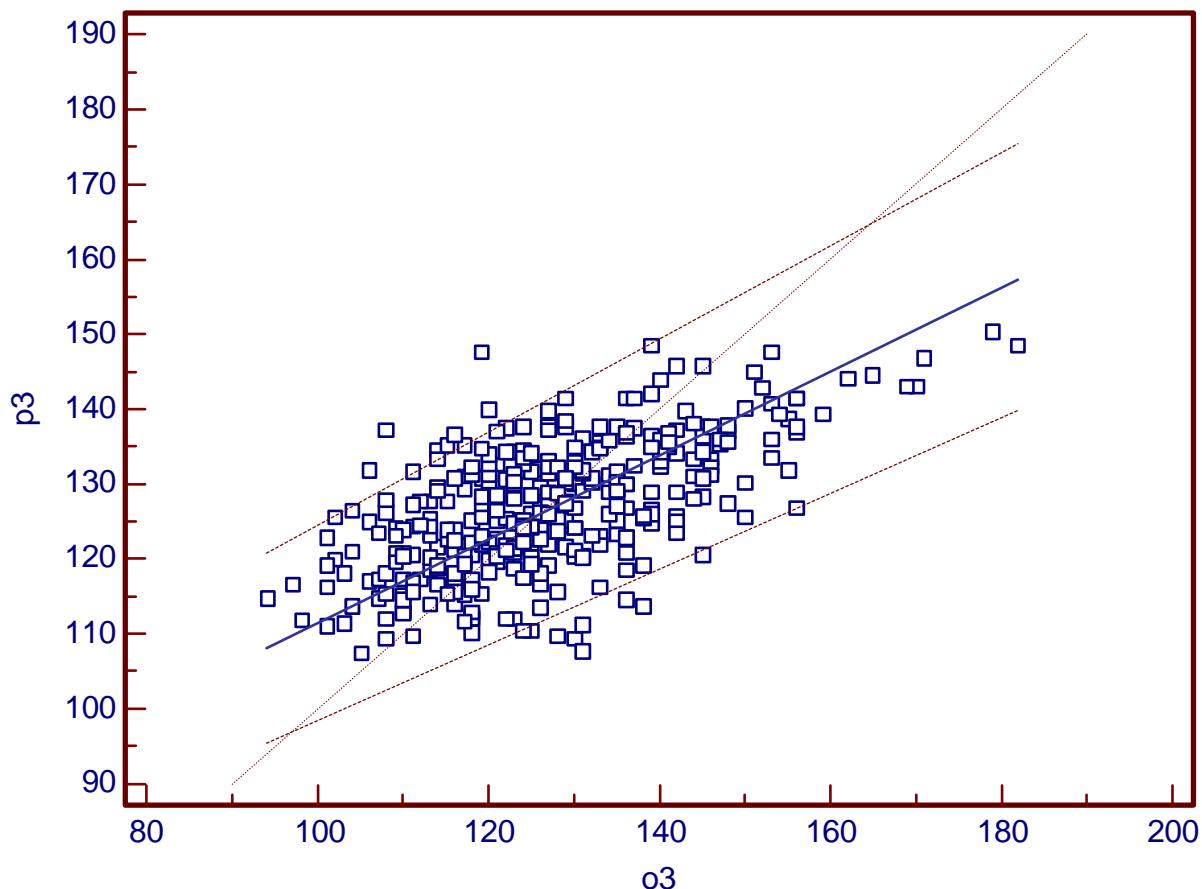


Figure 11. Regression graphic.



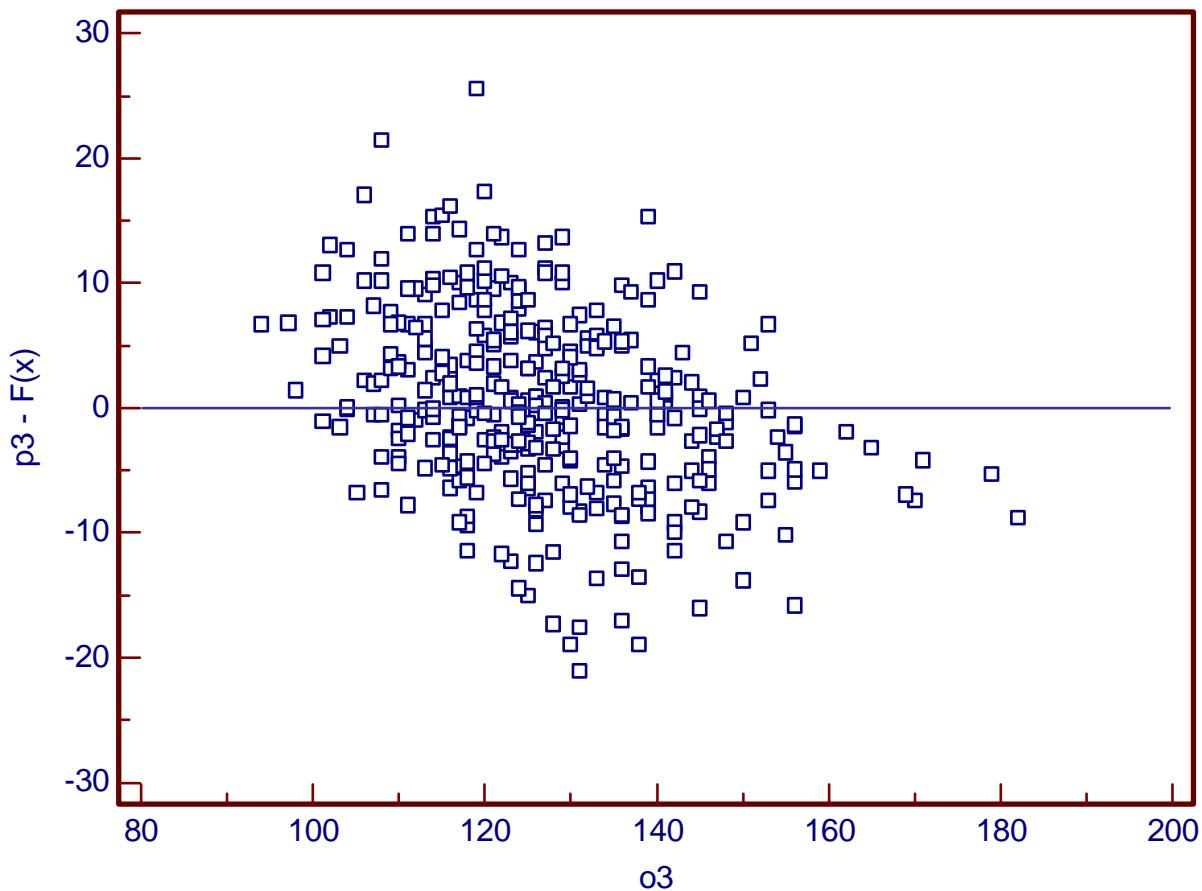


Figure 12. Residuals.

Table 4.

#### Passing and Bablok regression

<b>Variable X</b>	<b>o3</b>
<b>Variable Y</b>	<b>p3</b>
<b>Sample size</b>	<b>358</b>
<b>Lowest value</b>	<b>94.0000</b>
<b>Highest value</b>	<b>182.0000</b>
<b>Arithmetic mean</b>	<b>126.8296</b>
<b>Median</b>	<b>125.0000</b>
<b>Standard deviation</b>	<b>14.3348</b>
<b>Standard error of the mean</b>	<b>0.7576</b>

#### Regression Equation

$$y = 55.5390 + 0.5587 \times x$$

<b>Intercept A</b>	<b>55.5390</b>
<b>95% CI</b>	<b>47.8924 to 62.5786</b>
<b>Slope B</b>	<b>0.5587</b>
<b>95% CI</b>	<b>0.5048 to 0.6199</b>
<b>Cusum test for linearity</b>	<b>Significant deviation from linearity (P&lt;0.05)</b>

- Passing & Bablok regression

Visit 6

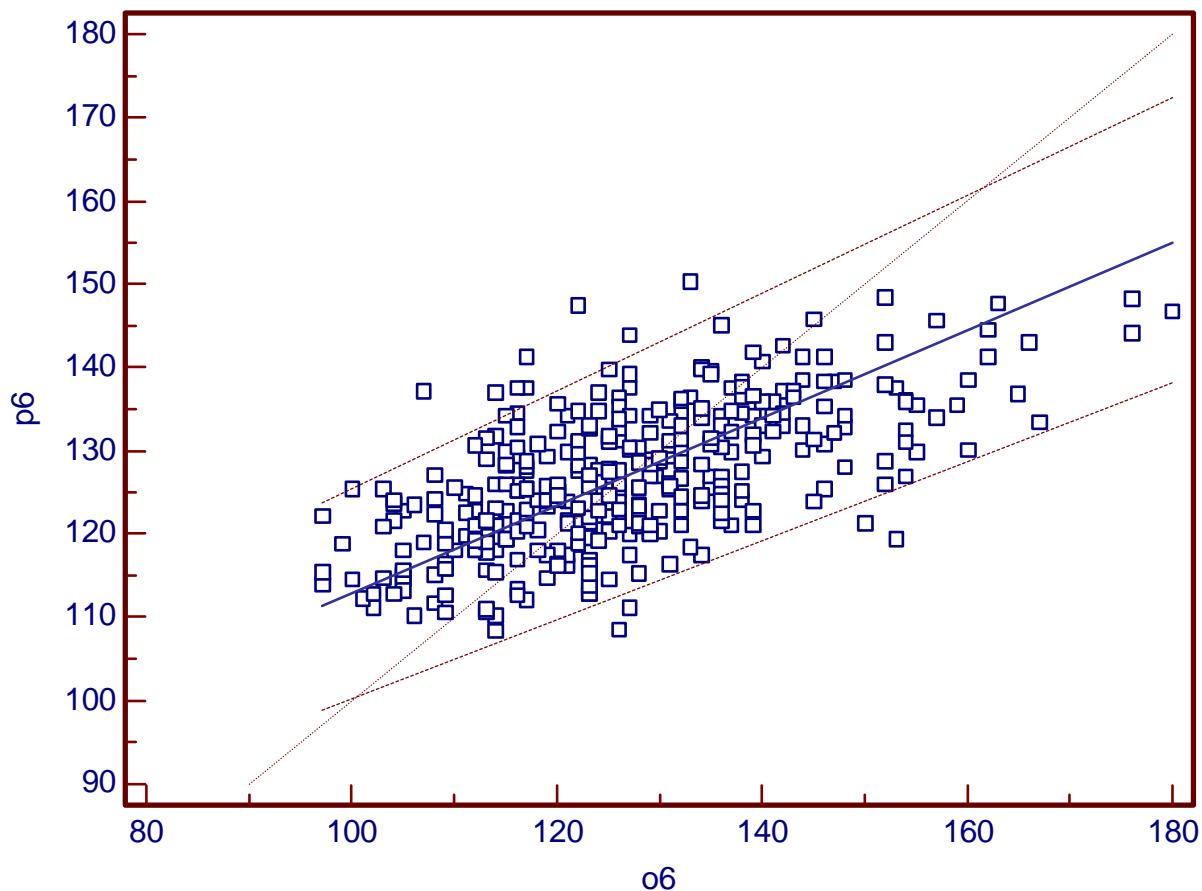


Figure 13. Regression graphic.



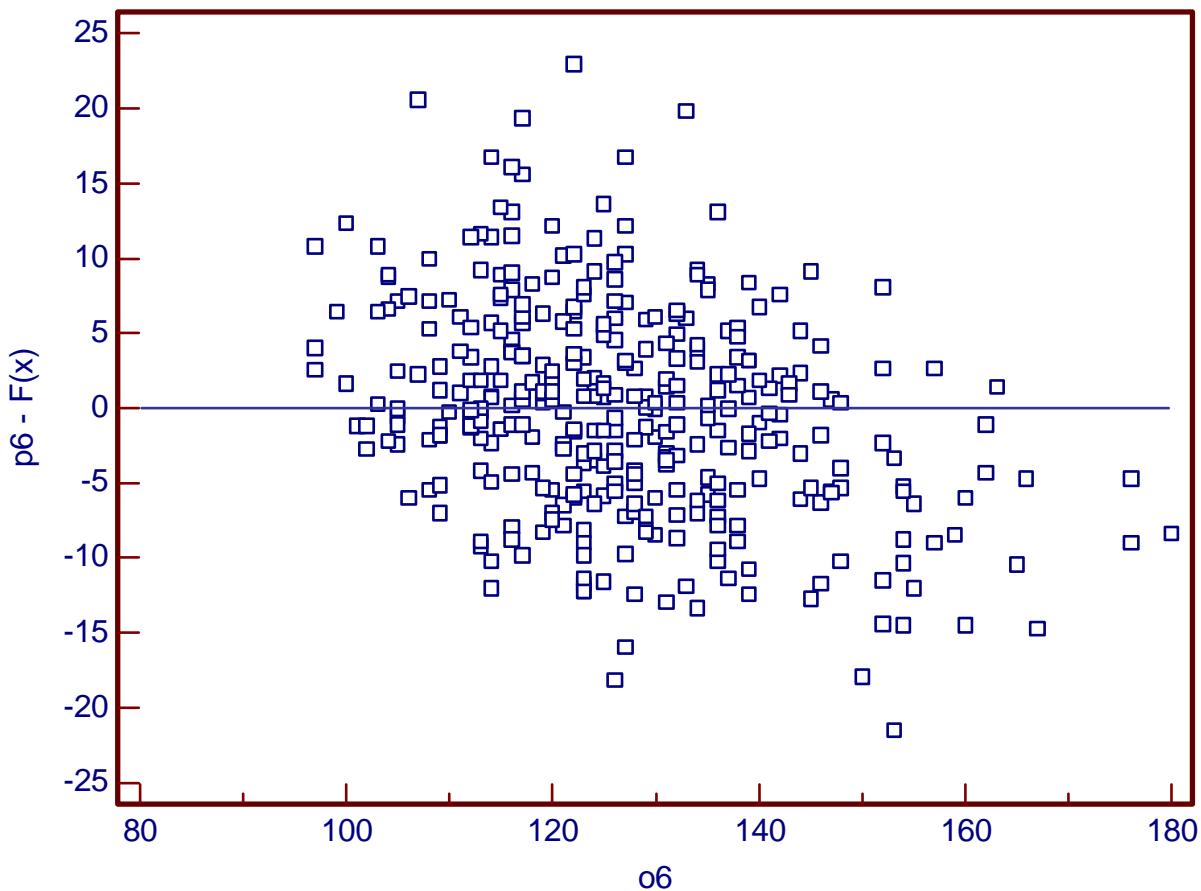


Figure 14. Residuals.  
Table 5.

#### Passing and Bablok regression

Variable X	<b>o6</b>	
Variable Y	<b>p6</b>	
Sample size	<b>352</b>	
	Variable X	Variable Y
Lowest value	<b>97.0000</b>	<b>108.3296</b>
Highest value	<b>180.0000</b>	<b>150.2912</b>
Arithmetic mean	<b>126.9773</b>	<b>127.0215</b>
Median	<b>125.0000</b>	<b>126.0914</b>
Standard deviation	<b>14.8742</b>	<b>8.5478</b>
Standard error of the mean	<b>0.7928</b>	<b>0.4556</b>

Regression Equation

$$y = 60.2810 + 0.5269 \times x$$

Intercept A	<b>60.2810</b>
95% CI	<b>52.8878 to 66.9507</b>
Slope B	<b>0.5269</b>
95% CI	<b>0.4738 to 0.5859</b>
Cusum test for linearity	<b>Significant deviation from linearity (P&lt;0.05)</b>

- Passing & Bablok regression

Visit 9

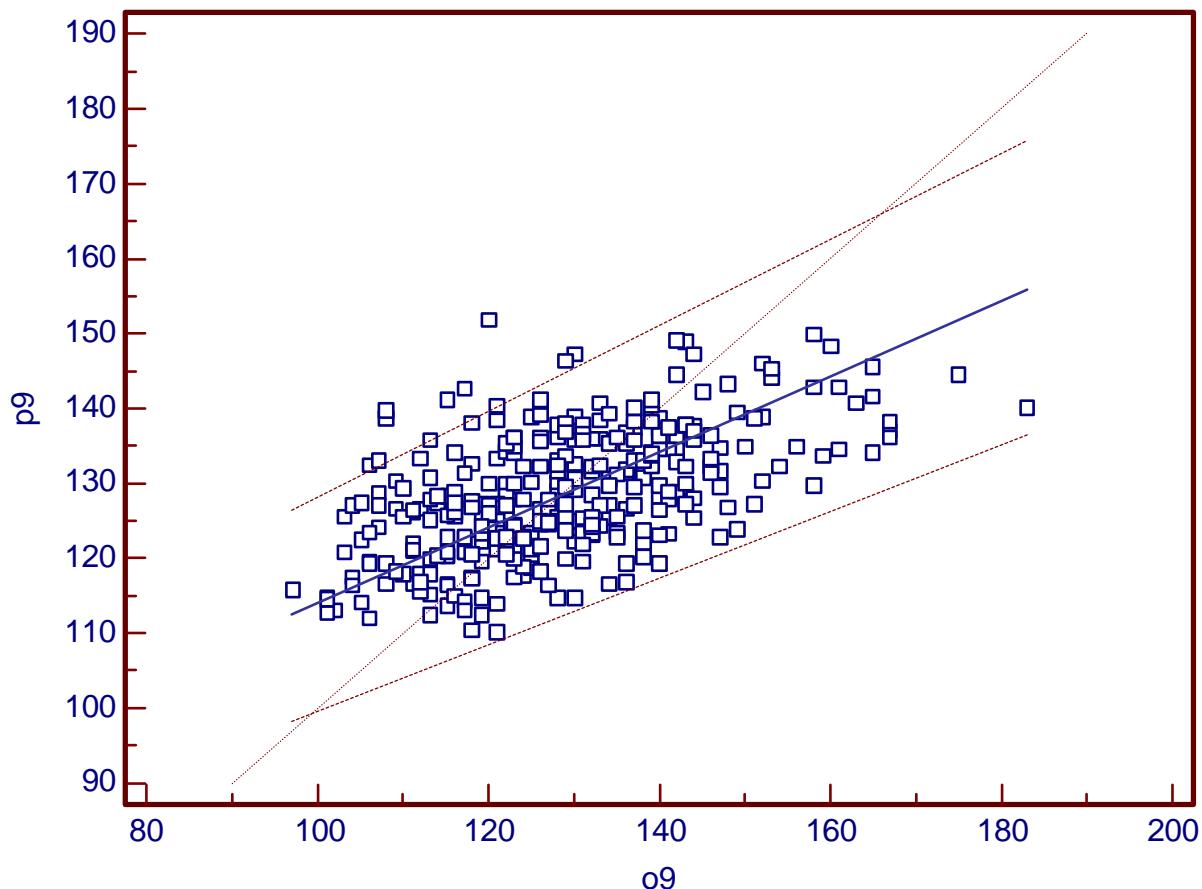


Figure 15. Regression graphic.



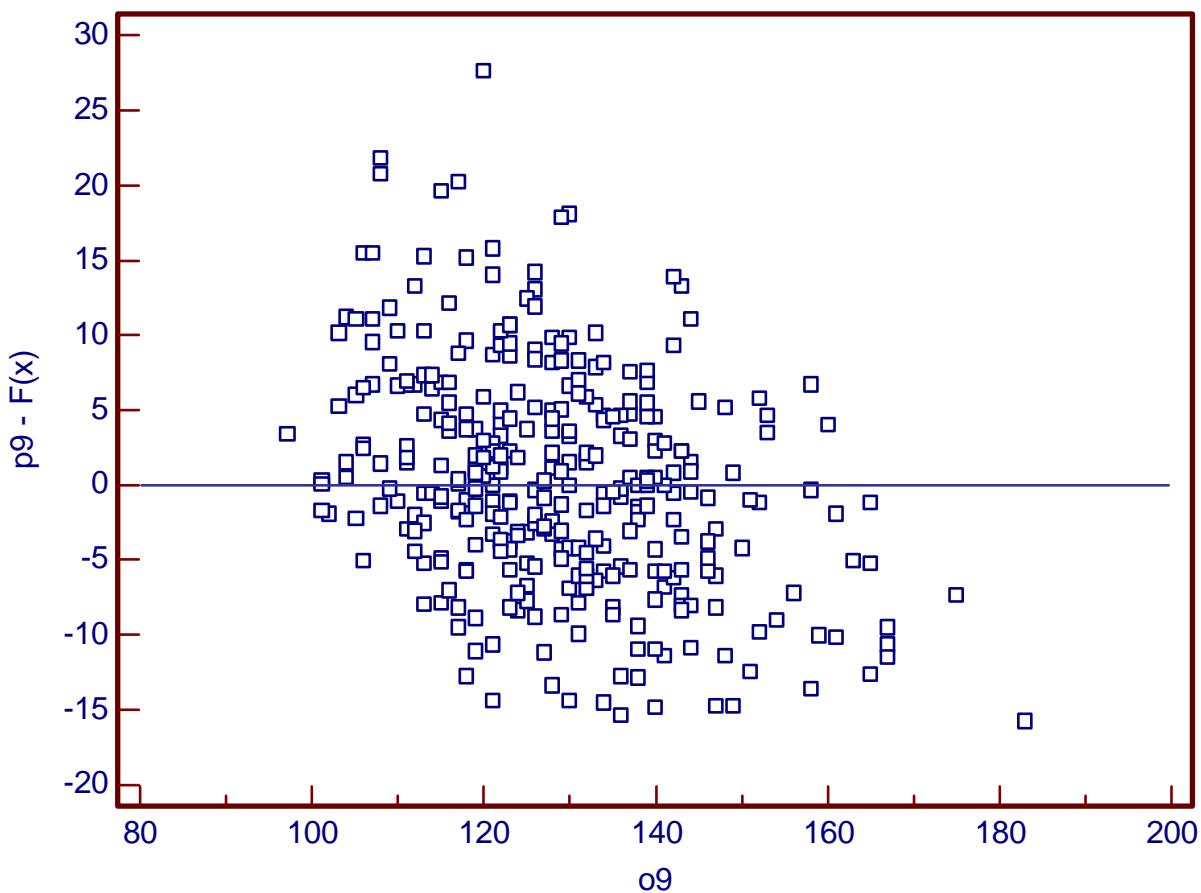


Figure 16. Residuals.

Table 6.

#### Passing and Bablok regression

Variable X	<b>o9</b>	
Variable Y	<b>p9</b>	
Sample size	<b>334</b>	
	Variable X	Variable Y
Lowest value	<b>97.0000</b>	<b>110.1637</b>
Highest value	<b>183.0000</b>	<b>151.7821</b>
Arithmetic mean	<b>128.5659</b>	<b>128.7128</b>
Median	<b>128.0000</b>	<b>127.8773</b>
Standard deviation	<b>14.6536</b>	<b>8.3858</b>
Standard error of the mean	<b>0.8018</b>	<b>0.4588</b>

#### Regression Equation

$$y = 63.3738 + 0.5056 \times x$$

Intercept A	<b>63.3738</b>
95% CI	<b>54.7833 to 71.0880</b>
Slope B	<b>0.5056</b>
95% CI	<b>0.4467 to 0.5719</b>
Cusum test for linearity	<b>No significant deviation from linearity (P&gt;0.10)</b>

- Mountain Plot

Visit 3

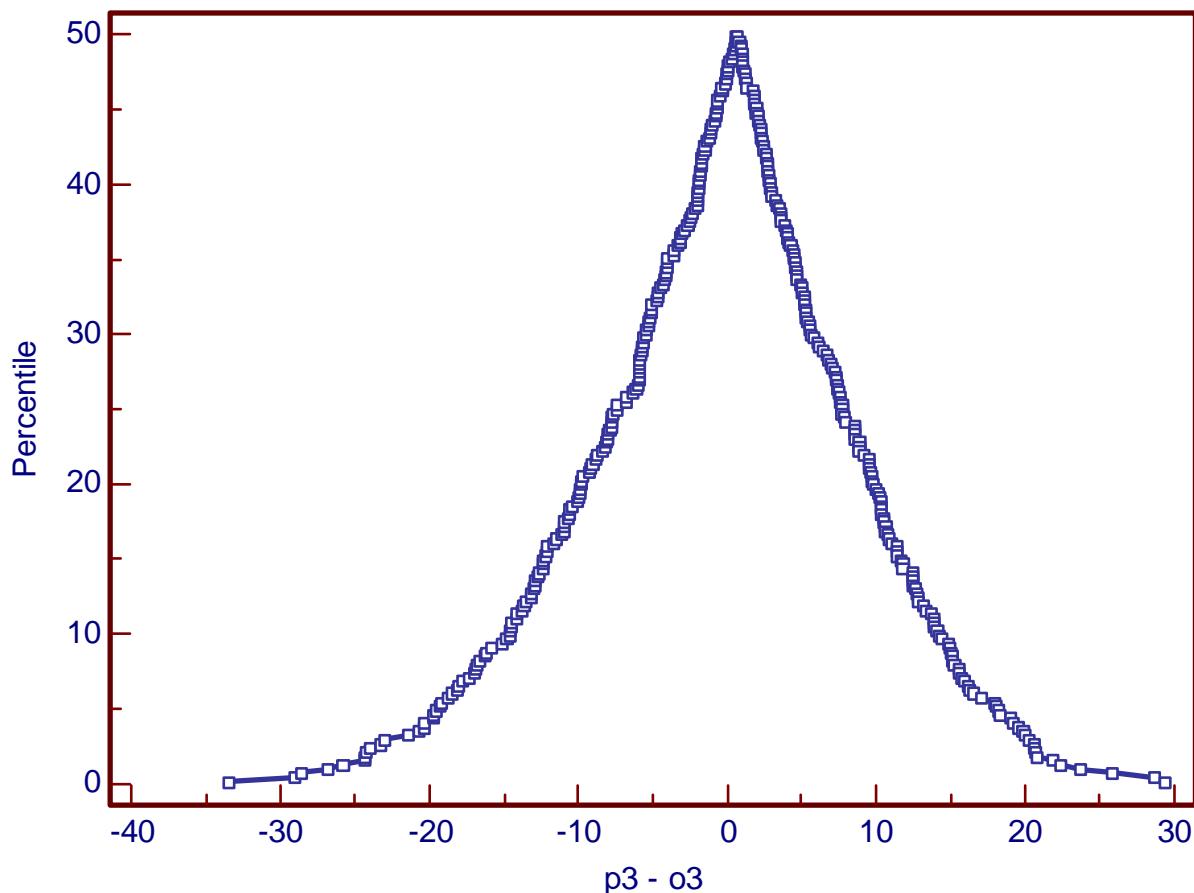


Figure 17.



- Mountain Plot

Visit 6

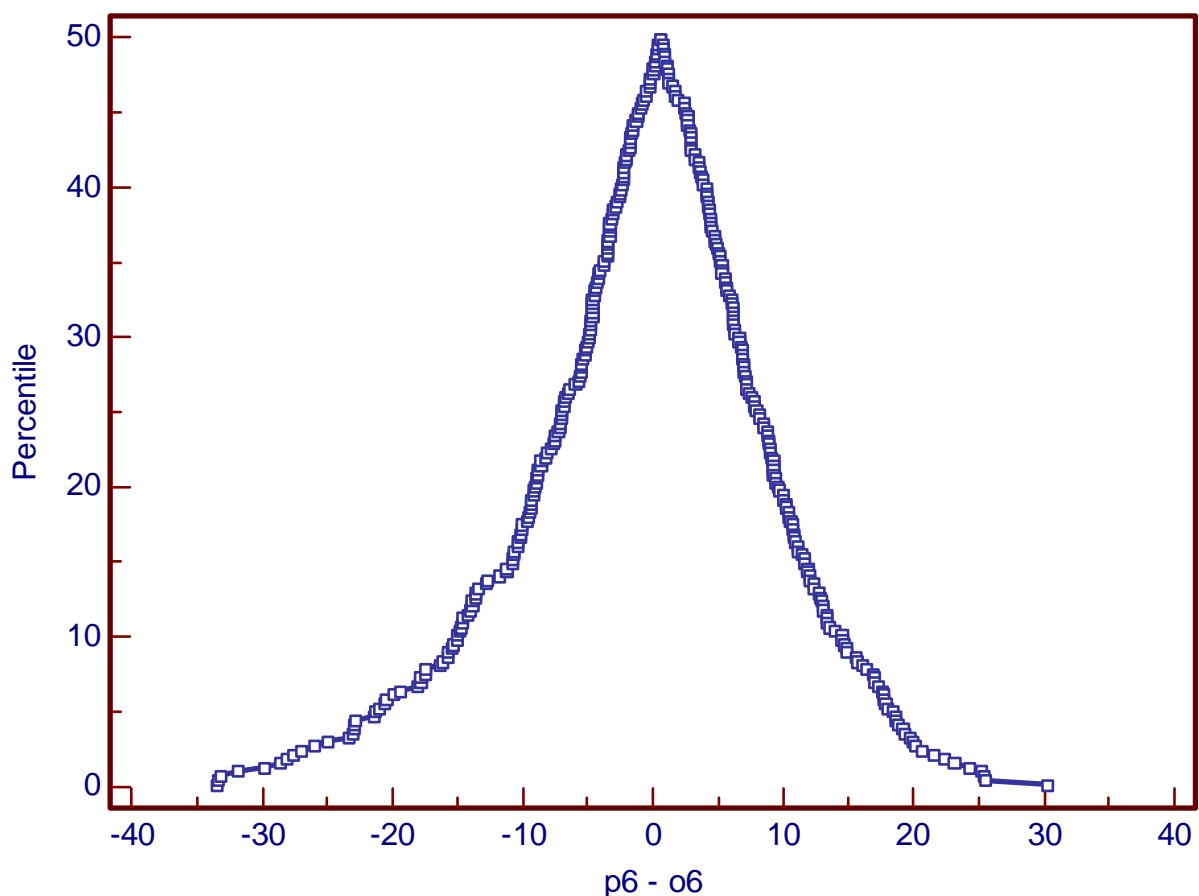
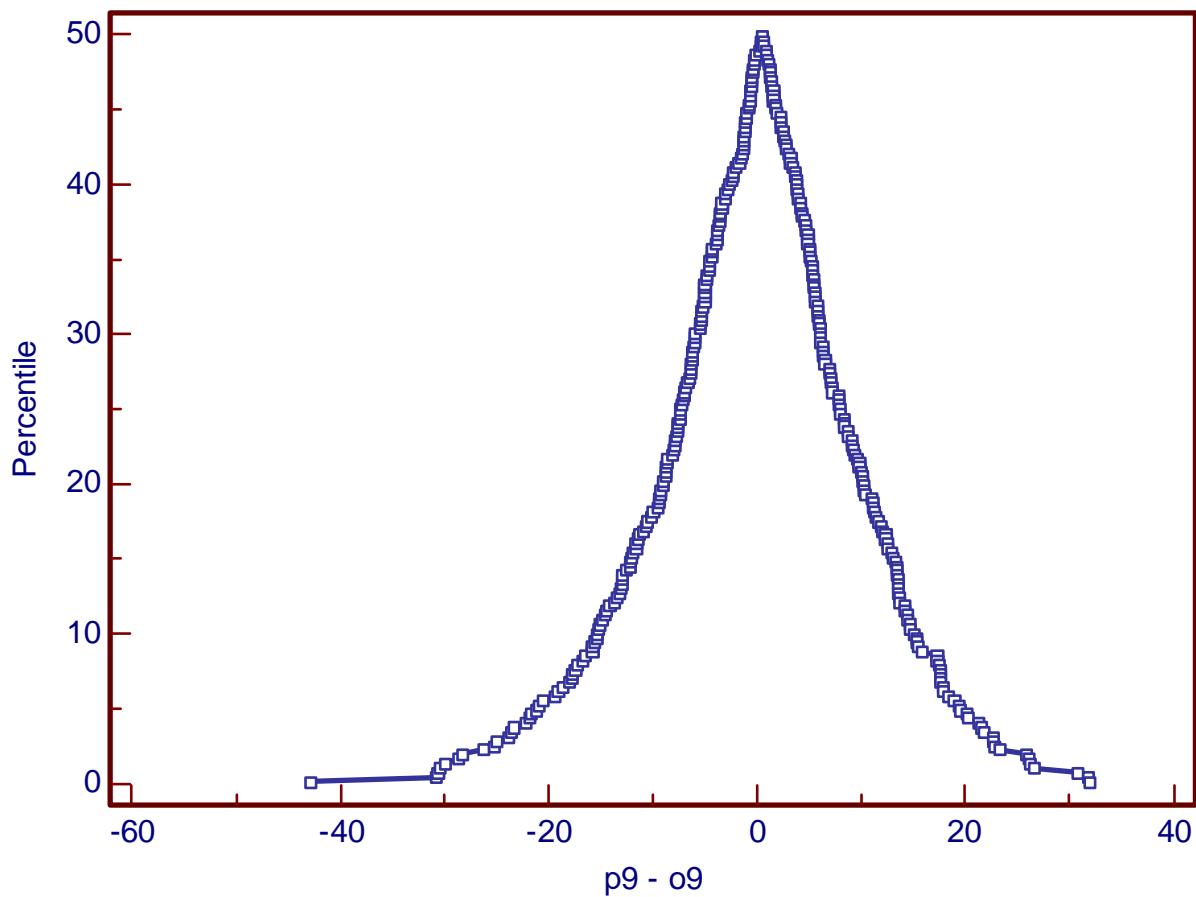


Figure 18.



- Mountain Plot

Visit 9



- Figure 19.



- Concordance Correlation Coefficient (CCC)

Visit 3

Table 7.

Concordance correlation coefficient	
-------------------------------------	--

Variable Y	p3
Variable X	o3
Sample size	358
Concordance correlation coefficient	<b>0.5549</b>
95% Confidence interval	<b>0.4919 to 0.6122</b>
Pearson $\rho$ (precision)	<b>0.6234</b>
Bias correction factor $C_b$ (accuracy)	<b>0.8902</b>

Concordance correlation coefficient	
-------------------------------------	--

Variable Y	p3 (Log)
Variable X	o3 (Log)
Sample size	358
Concordance correlation coefficient	<b>0.5492</b>
95% Confidence interval	<b>0.4845 to 0.6078</b>
Pearson $\rho$ (precision)	<b>0.6119</b>
Bias correction factor $C_b$ (accuracy)	<b>0.8974</b>



- Concordance Correlation Coefficient (CCC)

Visit 6

Table 8.

Concordance correlation coefficient	
Variable Y	p6
Variable X	o6
Sample size	352
Concordance correlation coefficient	0.5391
95% Confidence interval	0.4768 to 0.5960
Pearson $\rho$ (precision)	0.6240
Bias correction factor $C_b$ (accuracy)	0.8640

Concordance correlation coefficient	
Variable Y	p6 (Log)
Variable X	o6 (Log)
Sample size	352
Concordance correlation coefficient	0.5415
95% Confidence interval	0.4787 to 0.5989
Pearson $\rho$ (precision)	0.6220
Bias correction factor $C_b$ (accuracy)	0.8706



- Concordance Correlation Coefficient (CCC)

Visit 9

Table 9.

Concordance correlation coefficient	
Variable Y	p9
Variable X	o9
Sample size	334
Concordance correlation coefficient	0.4806
95% Confidence interval	0.4103 to 0.5452
Pearson $\rho$ (precision)	0.5574
Bias correction factor $C_b$ (accuracy)	0.8621

Concordance correlation coefficient	
Variable Y	p9 (Log)
Variable X	o9 (Log)
Sample size	334
Concordance correlation coefficient	0.4832
95% Confidence interval	0.4127 to 0.5481
Pearson $\rho$ (precision)	0.5580
Bias correction factor $C_b$ (accuracy)	0.8660



## Discussion

For each visit, we performed a ‘method of comparison’ analysis to assess the degree of concordance between observed and predicted values of the mixed-effect model. The mixed-effect model predicted sbp at visits 3, 6 and 9 based on sbpbl and trt.

The Predicted and Observed Values graphic in Figure 1 seems to indicate that the mean observed value and the mean predicted value at visit 3 are essentially the same. The lack of agreement increases thereafter. At visit 6 the difference is obvious and more so at visit 9. Thus, it appears that the model can predict sbp at visit 3 fairly well, but the further out the prediction, the less concordance we seem to see.

The Bland Altman plots do a better job of showing how concordant the observed and predicted values are at each visit (Figures 2,3 and 4). Specifically, we now see the degree of concordance between each observed and predicted value at a specific visit. In addition, we see how concordant the predicted values for specific observed values. Allowing us to assess measurement error and bias. The Bland Altman plots show that a small number of the matched pairs of observed and predicted values cluster near delta=0 (perfect agreement between the two readings would result in a delta=0). A number of deltas (predicted minus observed) appear to be equally distributed across the delta=0 line from the average of the predicted and the observed on the interval between 100 and about 140 (horizontal axis) indicating that there is no systematic bias in the matched readings. However, when the average of the predicted and the observed falls above 140, we see an obvious problem, the majority of the deltas are below the delta=0 line. This indicates some sort of systematic bias between the observed value and the model-based predicted value. Some of the deltas are negative, indicating that the observed value was larger than the matched predicted value. Some of the deltas are positive, indicating that the predicted value was larger than the matched observed value. The plots also show the variability associated with the deltas, with a number of matched values falling outside the +1.96 SD limit. Overall, at each visit, we see a less than satisfactory agreement between the predicted values and the observed values.

The Deming regression plots and tables (Figures 5,6,7,8,9,10 and Tables 1,2,3) show the same thing as the Bland Altman plots (Figures 2,3, and 4). A small number of the matched pairs of observed and predicted values cluster near the ‘line of equality’ (perfect agreement between the matched pair of predicted and observed values would sit directly on the ‘line of equality’). The “line of equality” is the diagonal red line at 45 degrees shown in Deming regression figures. The Deming regression line (the blue line in the Deming regression figures) shows the same bias we saw with the Bland Altman plots: when the observed value falls below approximately 130, the Deming regression line falls above the ‘line of equality’; and when the observed value falls above approximately 130, the Deming regression line falls below the ‘line of equality’. This indicates some sort of systematic bias between the observed value and the model-based predicted value. Tables 1,2, and 3 provide the actual Deming regression models which can be used to quantify this bias. Overall, at each visit, we see a less than satisfactory agreement between the predicted values and the observed values.

The Passing-Bablok regression plots and tables (Figures 11,12,13,14,15,16 and Tables 4,5,6) illustrate the same findings found by Deming regression. Overall, at each visit, we see a less than satisfactory agreement between the predicted values and the observed values.

The mountain plots (Figures 17,18, and 19) further support the findings of the Bland Altman plots, The Deming regression plots and tables, and the Passing-Bablok regression plots and tables. Again, overall, at each visit, we see a less than satisfactory agreement between the predicted values and the observed values.

The concordance correlation coefficient (CCC) estimates (Tables 7,8, and 9), for both original and log transformed observed and predicted values, further support of our conclusion that the degree of concordance between the observed and predicted values is less than satisfactory. At visit 3, the 95% confidence interval of the CCC was [0.4919, 0.6122] with the point estimate equal to 0.5549. At visit 6, the 95% confidence interval of the CCC was [0.4768, 0.5960] with the point estimate equal to 0.5391. At visit 9, the 95% confidence interval of the CCC was [0.4103, 0.5452] with the point estimate equal to

0.5574. There was very little difference between in the CCC estimates for both the original and log transformed values.

### **Conclusion**

We believe that the ‘method of comparison’ techniques provide a useful and informative way to assess the degree of concordance between observed and the model-based predicted values of a mixed-effect model. One can qualitatively assess the degree of concordance with visual inspection of the various graphics produced. One can also quantify the degree of concordance by using the Deming regression models and/or the Passing-Bablok regression models. In addition, one can use the concordance correlation coefficient (CCC) estimates to quantify the degree of concordance.



## References

- Akaike H. (1974), "A New Look at the Statistical Model Identification," IEEE Transaction on Automatic Control, AC - 19, 716 - 723.
- Bland JM and Altman DG (1986). Statistical Methods for Assessing Agreement between Two Methods of Clinical Measurement. *Lancet*, Feb 8; 1 (8476): 307-10.
- Altman D.G. and Bland J.M. (1983). Measurement in Medicine: The Analysis of Method Comparison Studies, *The Statistician*, 32, 307-317.
- Bland J.M. and Altman D.G. (1999). Measuring Agreement in Method Comparison Studies, *Statistical Methods in Medical Research*, 8, 135-160.
- Bozdogan H. (1987), "Model Selection and Akaike's Information Criterion (AIC): The General Theory and Its Analytical Extensions," *Psychometrika*, 52, 345 - 370.
- Burnham K.P. and Anderson D.R. (1998), *Model Selection and Inference: A Practical Information-Theoretic Approach*, New York: Springer-Verlag.
- Combleet PJ, Gochman N (1979) Incorrect Least-squares Regression Coefficients in Method-comparison Analysis. *Clinical Chemistry*, 25:432-438.
- Gönen M and Heller G (2005) Concordance Probability and Discriminatory Power in Proportional Hazards Regression. *Biometrika*, 92, 4, pp 965-970.
- Hannan E.J. and Quinn B.G. (1979), "The Determination of the Order of an Autoregression," *Journal of the Royal Statistical Society, Series B*, 41, 190 - 195.
- Harrell F.E., Califf R.M., Pryor D.B., Lee K.L. and Rosati R.A. (1982) Evaluating the Yield of Medical Tests. *JAMA*, 247, 2543-2546.
- Harrell F.E., Lee K.L., Califf R.M., Pryor D.B., and Rosati R.A. (1984) Regression Modeling Strategies for Improved Prognostic Prediction. *Statistics in Medicine*, 3, pp 143-152.
- Hurvich C.M. and Tsai C.-L. (1989), "Regression and Time Series Model Selection in Small Samples," *Biometrika*, 76, 297 - 307.
- King TS, Chinchilli VM and Carrasco JL (2007). A Repeated Measures Concordance Correlation Coefficient. *Statistics in Medicine*, 26, 3095-3113.
- Krouwer JS, Monti KL (1995) A Simple, Graphical Method to Evaluate Laboratory Assays. *Eur J Clin Chem Clin Biochem*, 33:525-527.
- Lin, LI (1989). A Concordance Correlation Coefficient to Evaluate Reproducibility. *Biometrics* 45, 255-268.
- Passing H, Bablok W (1983) A New Biometrical Procedure for Testing the Equality of Measurements from Two Different Analytical Methods. Application of Linear Regression Procedures for Method Comparison Studies in Clinical Chemistry, Part I. *J. Clin. Chem. Clin. Biochem.*, 21:709-720.
- Ross R.A., Lee M.L.T., Delaney M.L. and Onderdonk A.B. (1994) Mixed-effect Models for Predicting Microbial Interactions in the Vaginal Ecosystem. *Journal of Clinical Microbiology*, 32, 4, pp 871-875.
- Schwarz G. (1978), "Estimating the Dimension of a Model," *Annals of Statistics*, 6, 461 - 464.
- Vonesh EF, Chinchilli VM, Pu K. (1996). Goodness-of-fit in Generalized Nonlinear Mixed-effect Models. *Biometrics*, 52: 572-587.

## Appendix A. Data Set for Example

A	1	2	1	144.0	113	117	122
A	1	1	1	133.0	116	114	125
A	2	1	1	136.0	112	105	113
A	2	2	1	127.5	122	111	122
A	2	1	1	121.5	108	106	106
A	2	2	0	159.0	129	137	139
A	1	1	1	145.5	130	111	136
A	2	2	1	145.0	117	116	113
A	2	2	1	121.0	117	121	124
A	2	2	0	162.0	159	127	133
A	1	2	1	148.0	134	115	136
A	1	2	1	122.5	118	109	.
A	2	2	1	143.0	145	115	158
A	2	1	1	135.5	106	113	106
A	1	2	1	150.0	144	146	130
A	2	2	1	155.0	132	134	128
A	1	1	1	136.5	127	127	123
A	2	1	1	137.0	126	122	115
A	1	2	1	154.0	140	142	161
A	2	2	1	126.0	125	112	115
A	2	1	1	134.0	133	123	125
A	1	1	0	139.0	117	128	.
A	1	2	1	148.5	150	160	138
A	2	2	1	160.0	145	153	152
A	2	1	1	126.5	123	123	128
A	1	2	1	131.5	123	128	.
A	1	1	1	127.0	116	119	115
A	2	2	1	160.0	124	127	130
A	2	2	1	143.5	121	115	122
A	1	2	1	145.5	125	123	120
A	2	2	1	129.0	118	118	118
A	2	1	1	121.5	130	114	.
A	1	2	1	137.5	109	138	103
A	2	2	1	154.0	124	136	134
A	1	1	1	170.5	127	144	121
A	1	2	1	139.5	118	138	112
A	2	1	1	143.5	123	124	149
A	1	1	1	135.5	113	153	121
A	1	2	1	164.0	155	160	183
A	2	2	1	135.0	125	134	134
A	2	2	1	133.0	136	139	133
A	2	2	0	137.0	142	135	104
A	2	2	0	137.5	125	116	114
A	1	2	1	135.5	133	122	123
A	2	2	1	140.5	126	130	.
A	2	1	1	124.5	101	108	115
A	2	2	1	119.0	110	105	111
A	1	1	1	129.5	119	123	112
A	2	1	1	149.5	129	117	119
A	1	2	1	141.5	104	131	118
A	1	2	1	142.5	156	135	143
A	2	2	1	146.0	130	137	138
A	2	2	1	138.0	126	131	134
A	1	2	1	166.0	127	135	115
A	1	1	1	143.0	121	128	144
A	1	1	1	128.5	94	113	123
A	2	2	1	140.5	136	125	140

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A	2	1	1	130.0	113	103	108
A	2	2	0	149.0	140	147	159
A	1	2	1	160.5	156	139	118
A	2	2	1	154.5	114	116	133
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B	2	2	0	148.5	156	.	.
B	2	1	1	144.0	135	124	122
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B	1	1	1	130.0	118	110	129
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B	2	2	1	130.5	119	131	154
B	1	2	1	127.0	112	124	.
B	2	2	1	131.0	117	122	106
B	1	2	1	131.5	129	144	147
B	2	2	1	127.0	134	132	125
B	1	1	1	122.5	110	97	97
B	2	2	1	122.0	108	115	105
B	2	2	1	142.5	142	142	140
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B	1	2	1	139.0	123	121	130
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B	1	2	1	160.0	142	157	130
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B	2	2	1	141.0	145	126	128
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B	1	1	0	136.0	124	115	119
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B	2	2	1	136.5	142	134	134
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B	2	2	1	137.0	122	115	113
B	1	1	1	159.5	144	129	132
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B	2	2	1	138.0	141	124	123
B	2	2	1	128.0	135	140	138
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B	1	2	1	153.0	139	139	148
B	2	2	1	140.0	140	141	137
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B	1	2	1	152.0	156	162	.
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B	1	1	1	136.5	109	116	121
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B	2	2	1	152.5	152	142	153
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B	2	1	0	153.0	114	116	146
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B	2	2	1	129.5	132	127	132
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B	1	2	1	134.0	111	113	107
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B	1	2	1	131.0	136	122	117
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B	2	1	1	148.0	122	.	.
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B	2	2	1	141.0	136	138	143
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B	2	1	1	133.0	107	120	123
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B	1	2	1	133.5	120	126	130

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B	1	1	1	143.0	111	116	107
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C	2	2	1	144.5	135	135	137
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C	2	1	1	161.0	126	148	147
C	1	2	1	146.5	125	125	128
C	2	2	1	169.0	151	136	129
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C	2	2	1	160.0	150	134	165
C	2	2	1	146.5	124	126	165
C	2	2	1	138.0	123	117	137
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C	1	1	1	132.5	108	109	103
C	2	1	1	160.0	123	141	116
C	2	2	1	136.0	127	129	132
C	2	1	1	142.0	114	117	123
C	1	2	1	152.5	130	122	146
C	2	2	1	151.0	115	134	131
C	2	2	1	153.5	116	143	129
C	1	1	1	145.0	142	.	.
C	1	2	1	131.5	113	119	128
C	1	1	1	133.5	114	115	125
C	2	1	1	148.0	106	136	143
C	1	1	1	137.5	136	126	135
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C	2	2	1	170.5	145	145	144
C	1	2	1	131.0	113	114	120
C	1	1	1	143.0	116	125	140
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C	1	2	1	124.5	109	113	111
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C	2	2	1	143.5	118	125	128
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C	2	2	0	154.5	148	138	134
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C	1	2	1	125.0	102	113	111
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C	2	1	1	139.5	130	139	147
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C	2	1	1	138.0	117	116	130
C	1	2	1	128.5	133	104	141
C	2	1	0	142.0	132	145	121

C	2	2	0	137.5	121	134	123
C	2	1	1	124.0	98	116	101
C	1	1	1	139.5	127	132	126
C	2	2	1	139.5	139	152	152
C	2	2	1	137.5	108	125	110
C	2	2	1	130.5	126	119	119
C	2	2	1	138.0	144	148	147
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C	2	1	1	140.0	145	123	119
C	2	2	1	132.0	123	136	111
C	2	2	0	172.5	153	163	142
C	2	1	1	135.5	116	107	117
C	2	2	0	143.5	131	125	112
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C	2	2	1	145.5	130	129	139
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C	1	2	1	154.0	134	120	140
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C	2	2	1	125.0	104	103	105
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C	1	1	1	158.5	127	132	150
C	1	2	1	136.0	134	119	121
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C	2	1	1	148.5	124	131	124
C	2	2	1	135.0	121	124	113
C	2	1	1	171.0	137	146	137
C	2	1	0	161.0	124	127	126
C	1	1	1	168.5	146	148	139
C	2	2	1	146.5	120	123	123
C	2	2	1	167.0	140	127	153
C	1	1	1	141.0	126	106	131
C	2	1	1	139.5	110	112	122
C	2	2	1	143.5	146	154	133
C	2	1	1	140.5	121	113	106
C	1	2	1	137.5	139	132	144
C	1	2	1	136.0	139	123	143
C	2	1	1	161.5	118	123	123
C	1	2	1	161.5	143	125	139
C	2	2	1	133.0	128	100	148
C	2	2	1	133.0	113	103	121
C	2	2	1	148.5	120	126	122
C	1	2	1	125.5	113	129	126
C	2	1	1	116.0	105	114	121
C	2	2	1	143.0	116	118	124

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C	1	1	1	128.0	116	120	126
D	2	2	0	132.5	125	136	132
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D	2	1	1	120.5	128	113	113
D	1	2	1	144.0	125	128	143
D	2	1	1	151.5	130	126	129
D	1	1	0	132.0	138	129	131
D	1	2	0	149.5	128	120	.
D	1	2	1	156.5	147	146	129
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D	2	2	1	155.5	153	140	141
D	1	2	0	166.0	129	117	117
D	2	2	0	127.5	123	121	115
D	2	2	1	146.0	129	112	126
D	2	2	1	136.0	138	120	118
D	2	1	1	147.0	113	120	122
D	2	1	1	121.0	118	113	101
D	1	2	0	143.0	128	.	.
D	1	2	0	134.0	110	104	113
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D	1	1	1	132.5	116	122	118
D	2	2	1	124.5	101	113	114
D	2	2	0	123.5	114	112	122
D	2	2	1	152.0	125	157	126
D	2	1	1	131.0	128	131	109
D	2	2	1	158.5	133	116	126
D	2	1	1	120.5	111	109	119
D	2	1	1	124.5	108	102	119
D	2	2	0	152.0	119	137	123
D	1	1	0	118.5	117	109	117
D	2	2	1	125.0	125	124	115
D	2	2	0	158.0	144	152	149
D	2	1	1	130.5	115	120	113
D	1	1	1	140.5	116	122	126
D	1	2	1	138.5	119	110	120
D	2	2	1	137.0	138	131	151
D	2	2	1	134.0	125	118	110
D	2	2	1	165.5	137	146	158
D	1	2	1	148.0	145	139	143
D	1	1	1	135.0	117	122	.
D	1	1	1	142.0	109	104	115
D	2	2	1	157.0	136	139	139
D	2	1	1	145.5	107	108	116
D	1	2	1	141.0	135	154	114
D	2	2	1	155.5	147	154	.
D	2	2	1	128.5	130	126	124
D	2	1	1	167.5	148	132	137
D	1	2	1	136.5	124	132	120
D	2	1	1	140.0	121	150	140
D	2	2	1	131.5	119	124	119
D	1	2	1	134.0	119	126	132
D	2	1	1	121.5	124	127	117
D	2	2	0	132.5	124	119	129
D	2	2	1	118.0	111	97	112
D	2	2	0	136.0	127	120	116
D	2	1	1	147.5	112	117	129
D	2	2	0	129.0	124	97	129
D	2	2	0	132.5	130	120	135

D	1	2	1	130.5	122	132	.
D	2	2	1	132.5	142	128	127
D	2	1	1	139.5	131	129	117
D	2	2	1	152.5	145	148	137
D	1	2	0	118.5	108	123	136
D	2	1	0	143.5	128	120	111



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Appendix B. The resulting SAS output and SAS dataset for predictive validity assessment.

The Mixed Procedure

Model Information

Data Set	WORK.BP
Dependent Variable	sbp
Covariance Structure	Compound Symmetry
Subject Effect	person
Group Effect	trt
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
trt	2	1 2
visit	3	3 6 9
complier	2	0 1
clinic	4	A B C D
stratum	2	1 2

The Mixed Procedure

Class Level Information

Class	Levels	Values
person	358	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164 165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186

187	188	189	190	191	192	193
194	195	196	197	198	199	200
201	202	203	204	205	206	207
208	209	210	211	212	213	214
215	216	217	218	219	220	221
222	223	224	225	226	227	228
229	230	231	232	233	234	235
236	237	238	239	240	241	242
243	244	245	246	247	248	249
250	251	252	253	254	255	256
257	258	259	260	261	262	263
264	265	266	267	268	269	270
271	272	273	274	275	276	277
278	279	280	281	282	283	284
285	286	287	288	289	290	291
292	293	294	295	296	297	298
299	300	301	302	303	304	305
306	307	308	309	310	311	312
313	314	315	316	317	318	319
320	321	322	323	324	325	326
327	328	329	330	331	332	333
334	335	336	337	338	339	340
341	342	343	344	345	346	347
348	349	350	351	352	353	354
355	356	357	358			

#### Dimensions

Covariance Parameters	4
Columns in X	37
Columns in Z	0
Subjects	358
Max Obs Per Subject	3

#### Number of Observations

Number of Observations Read	1074
Number of Observations Used	1044
Number of Observations Not Used	30

#### Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	8060.04291931	
1	2	7886.53193967	0.00000001

#### The Mixed Procedure

#### Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
2	1	7886.53190834	0.00000000



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Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
Variance	person	trt 1	69.0629
CS	person	trt 1	34.9670
Variance	person	trt 2	87.2927
CS	person	trt 2	71.7782

Fit Statistics

-2 Res Log Likelihood	7886.5
AIC (smaller is better)	7894.5
AICC (smaller is better)	7894.6
BIC (smaller is better)	7910.1

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
3	173.51	<.0001

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num	Den	F Value	Pr > F
	DF	DF		
sbpb1	1	345	194.84	<.0001
trt	1	345	21.38	<.0001
visit	2	682	4.90	0.0077
trt*visit	2	682	0.45	0.6393
complier	1	345	0.47	0.4914
trt*complier	1	345	0.05	0.8263
clinic	3	345	6.25	0.0004
trt*clinic	3	345	3.76	0.0112
stratum	1	345	0.06	0.8021
trt*stratum	1	345	1.86	0.1736



Obs	o3	o6	o9	person	p3	p6	p9
1	113	117	122	1	127.754	127.686	129.177
2	116	114	125	2	117.228	118.077	119.911
3	112	105	113	3	117.257	118.106	119.941
4	122	111	122	4	119.844	119.776	121.267
5	108	106	106	5	109.329	110.178	112.012
6	129	137	139	6	137.783	137.715	139.206
7	130	111	136	7	124.063	124.912	126.746
8	117	116	113	8	129.413	129.345	130.836
9	117	121	124	9	116.290	116.222	117.713
10	159	127	133	10	139.423	139.355	140.846
11	134	115	136	11	129.941	129.873	131.364
12	118	109	.	12	115.998	115.930	115.889
13	145	115	158	13	128.319	128.251	129.742
14	106	113	106	14	116.984	117.833	119.667
15	144	146	130	15	131.035	130.967	132.458
16	132	134	128	16	134.881	134.813	136.304
17	127	127	123	17	119.142	119.991	121.825
18	126	122	115	18	117.804	118.653	120.487
19	140	142	161	19	133.222	133.154	134.645
20	125	112	115	20	119.024	118.956	120.447
21	133	123	125	21	116.164	117.013	118.847
22	117	128	.	22	121.892	122.741	124.667
23	150	160	138	23	130.215	130.147	131.637
24	145	153	152	24	137.615	137.547	139.038
25	123	123	128	25	112.063	112.912	114.746
26	123	128	.	26	120.919	120.851	125.212
27	116	119	115	27	113.948	114.797	116.631
28	124	127	130	28	137.615	137.547	139.038
29	121	115	122	29	128.593	128.525	130.016
30	125	123	120	30	128.574	128.506	129.997
31	118	118	118	31	120.664	120.596	122.087
32	130	114	.	32	109.329	110.178	118.174
33	109	138	103	33	124.200	124.132	125.623
34	124	136	134	34	134.334	134.266	135.757
35	127	144	121	35	137.733	138.582	140.416
36	118	138	112	36	125.293	125.225	126.716
37	123	124	149	37	121.358	122.207	124.042
38	113	153	121	38	118.595	119.444	121.278
39	155	160	183	39	138.690	138.622	140.113
40	125	134	134	40	123.945	123.877	125.368
41	136	139	133	41	122.851	122.783	124.274
42	142	135	104	42	125.754	125.686	127.177
43	125	116	114	43	126.027	125.959	127.450
44	133	122	123	44	123.106	123.038	124.529
45	126	130	.	45	126.952	126.884	129.048
46	101	108	115	46	110.969	111.818	113.652
47	110	105	111	47	115.196	115.128	116.619
48	119	123	112	48	115.315	116.164	117.998
49	129	117	119	49	124.639	125.488	127.322
50	104	131	118	50	126.387	126.319	127.810
51	156	135	143	51	126.934	126.866	128.357
52	130	137	138	52	129.960	129.892	131.383
53	126	131	134	53	125.585	125.517	127.008
54	127	135	115	54	139.784	139.715	141.206
55	121	128	144	55	122.696	123.545	125.379

56	94	113	123	56	114.768	115.617	117.451
57	136	125	140	57	126.952	126.884	128.375
58	117	108	134	58	115.196	115.128	116.619
59	113	103	108	59	113.977	114.826	116.660
60	140	147	159	60	132.315	132.247	133.738
61	156	139	118	61	136.776	136.708	138.199
62	114	116	133	62	134.607	134.539	136.030
63	150	146	137	63	125.585	125.517	127.008
64	135	114	123	64	125.186	126.035	127.869
65	97	109	110	65	116.563	116.495	117.986
66	129	124	122	66	126.934	126.866	128.357
67	139	116	126	67	125.312	125.244	126.735
68	122	147	126	68	137.489	138.338	140.172
69	131	126	118	69	107.688	108.538	110.372
70	104	105	115	70	113.703	114.552	116.386
71	139	134	122	71	124.765	124.697	126.188
72	116	114	117	72	121.211	121.143	122.634
73	126	116	.	73	113.556	113.488	119.629
74	107	105	104	74	114.797	115.646	117.480
75	111	109	111	75	120.646	120.578	122.069
76	110	112	.	76	117.228	118.077	116.564
77	106	114	121	77	131.855	131.787	133.278
78	101	105	107	78	122.833	122.765	124.256
79	148	124	133	79	137.068	137.000	138.491
80	139	133	131	80	136.521	136.453	137.944
81	110	121	125	81	120.791	121.640	123.474
82	118	105	116	82	112.315	113.164	114.999
83	156	.	.	83	141.356	147.896	149.387
84	135	124	122	84	123.280	124.129	125.964
85	129	131	128	85	127.772	127.704	129.195
86	136	115	123	86	118.633	119.482	121.316
87	118	110	129	87	117.237	118.086	119.920
88	119	122	143	88	147.625	147.557	149.048
89	131	129	134	89	129.139	129.071	130.562
90	121	154	139	90	132.712	132.644	134.135
91	119	131	154	91	130.798	130.730	132.221
92	112	124	.	92	127.772	127.704	123.139
93	117	122	106	93	131.072	131.004	132.494
94	129	144	147	94	130.233	130.165	131.656
95	134	132	125	95	128.884	128.816	130.307
96	110	97	97	96	113.136	113.985	115.819
97	108	115	105	97	126.150	126.082	127.573
98	142	142	140	98	137.360	137.292	138.783
99	134	131	118	99	131.326	131.258	132.749
100	123	121	130	100	134.334	134.266	135.757
101	101	116	124	101	116.172	117.021	118.855
102	142	157	130	102	145.817	145.749	147.239
103	118	104	101	103	112.042	112.891	114.725
104	110	123	113	104	112.618	113.467	115.301
105	162	176	165	105	144.176	144.108	145.599
106	126	134	136	106	116.690	117.539	119.373
107	145	126	128	107	136.539	136.471	137.962
108	133	159	167	108	135.719	135.651	137.142
109	165	162	152	109	144.636	144.568	146.059
110	131	154	144	110	136.266	136.198	137.689
111	116	121	140	111	116.690	117.539	119.373
112	116	121	116	112	123.007	123.856	125.690
113	120	128	132	113	130.506	130.438	131.929
114	153	140	145	114	140.895	140.827	142.318
115	122	123	130	115	112.071	112.920	114.754

116	129	126	127	116	125.312	125.244	126.735
117	136	128	.	117	114.503	115.352	125.776
118	132	139	144	118	134.334	134.266	135.757
119	136	144	161	119	141.442	141.374	142.865
120	156	.	.	120	137.783	145.935	147.426
121	119	112	121	121	121.913	122.762	124.597
122	122	136	136	122	130.525	130.457	131.948
123	108	107	108	123	137.360	137.292	138.783
124	124	115	119	124	121.900	122.749	124.583
125	125	102	102	125	110.431	111.280	113.114
126	123	126	141	126	125.194	126.043	127.877
127	133	132	167	127	134.899	134.831	136.322
128	118	123	112	128	112.891	113.740	115.574
129	127	143	151	129	137.341	137.273	138.764
130	142	134	134	130	134.079	134.011	135.502
131	170	152	142	131	143.101	143.033	144.524
132	126	136	115	132	126.971	126.903	128.393
133	122	115	113	133	134.352	134.284	135.775
134	144	129	132	134	133.367	134.216	136.050
135	129	138	108	135	138.453	138.385	139.876
136	141	124	123	136	134.899	134.831	136.322
137	135	140	138	137	129.431	129.363	130.854
138	121	152	127	138	125.194	126.043	127.877
139	136	126	128	139	123.007	123.856	125.690
140	131	117	121	140	111.251	112.100	113.934
141	111	108	107	141	127.244	127.176	128.667
142	124	138	142	142	134.607	134.539	136.030
143	115	122	130	143	127.686	127.618	129.109
144	123	121	.	144	129.978	129.910	126.461
145	142	130	128	145	128.866	128.798	130.289
146	135	117	125	146	137.633	137.565	139.056
147	139	139	148	147	141.989	141.921	143.412
148	140	141	137	148	135.993	135.925	137.416
149	131	128	132	149	120.517	121.366	123.200
150	156	162	.	150	141.442	141.374	153.805
151	129	108	129	151	121.640	122.489	124.323
152	109	116	121	152	120.791	121.640	123.474
153	114	136	142	153	133.259	133.191	134.682
154	152	142	153	154	142.828	142.760	144.251
155	139	152	158	155	148.569	148.501	149.992
156	114	116	146	156	129.584	130.434	132.268
157	179	133	120	157	150.359	150.291	151.782
158	132	127	132	158	130.251	130.183	131.674
159	119	.	.	159	126.697	123.156	124.647
160	182	176	.	160	148.445	148.377	168.890
161	111	113	107	161	131.600	131.532	133.023
162	169	166	175	162	143.101	143.033	144.524
163	136	122	117	163	129.960	129.891	131.382
164	130	131	136	164	132.820	133.669	135.503
165	122	.	.	165	125.468	125.151	126.985
166	146	144	141	166	133.259	133.191	134.682
167	114	127	108	167	116.706	117.555	119.389
168	103	99	117	168	118.057	118.906	120.740
169	117	132	143	169	135.310	136.159	137.993
170	141	126	136	170	135.427	135.359	136.850
171	136	138	143	171	136.539	136.471	137.962
172	125	114	124	172	120.260	121.109	122.943
173	107	120	123	173	117.266	118.115	119.949
174	171	180	160	174	146.910	146.842	148.333
175	120	126	130	175	131.326	131.258	132.749

176	114	113	.	176	129.139	129.071	120.858
177	133	142	135	177	134.776	134.708	136.198
178	111	116	107	178	124.345	125.194	127.028
179	132	135	139	179	130.885	130.817	132.308
180	135	135	137	180	131.705	131.637	133.128
181	135	132	128	181	130.320	130.252	131.743
182	126	148	147	182	132.086	132.935	134.769
183	125	125	128	183	131.687	131.619	133.110
184	151	136	129	184	145.102	145.034	146.525
185	126	127	132	185	129.626	130.475	132.309
186	150	134	165	186	140.181	140.113	141.604
187	124	126	165	187	132.799	132.731	134.222
188	123	117	137	188	128.151	128.083	129.574
189	120	119	135	189	128.519	129.368	131.202
190	140	140	140	190	133.222	133.154	134.645
191	108	109	103	191	118.114	118.963	120.797
192	123	141	116	192	131.540	132.389	134.223
193	127	129	132	193	127.058	126.990	128.480
194	114	117	123	194	121.697	122.546	124.380
195	130	122	146	195	134.968	134.900	136.391
196	115	134	131	196	135.259	135.191	136.682
197	116	143	129	197	136.626	136.558	138.049
198	142	.	.	198	124.949	131.529	133.363
199	113	119	128	199	123.485	123.417	124.908
200	114	115	125	200	118.661	119.510	121.344
201	106	136	143	201	124.978	125.827	127.661
202	136	126	135	202	120.848	121.697	123.531
203	126	112	119	203	118.204	118.136	119.627
204	145	145	144	204	145.922	145.854	147.345
205	113	114	120	205	123.212	123.144	124.634
206	116	125	140	206	123.855	124.704	126.538
207	146	147	129	207	132.234	132.166	133.657
208	117	130	127	208	121.971	122.820	124.654
209	121	114	121	209	137.155	137.087	138.578
210	119	129	140	210	128.425	128.357	129.847
211	121	130	138	211	119.481	120.330	122.164
212	109	113	111	212	119.657	119.589	121.080
213	117	125	119	213	119.510	120.359	122.193
214	118	125	128	214	131.159	131.090	132.581
215	138	125	127	215	113.769	114.618	116.452
216	127	117	109	216	128.971	128.903	130.394
217	102	128	133	217	125.672	125.604	127.095
218	123	123	122	218	118.690	119.539	121.373
219	120	117	130	219	122.244	123.093	124.927
220	140	141	131	220	134.334	134.266	135.757
221	148	138	134	221	137.888	137.820	139.311
222	141	165	167	222	136.881	136.813	138.304
223	121	122	134	223	128.319	128.251	129.742
224	155	139	146	224	131.979	131.911	133.402
225	102	113	111	225	119.931	119.863	121.354
226	120	134	126	226	139.907	139.839	141.330
227	118	109	118	227	116.017	115.949	117.439
228	131	145	142	228	131.432	131.364	132.855
229	111	119	106	229	116.776	117.625	119.459
230	130	139	147	230	120.330	121.179	123.013
231	153	167	156	231	133.619	133.551	135.042
232	117	116	130	232	119.510	120.359	122.193
233	133	104	141	233	121.845	121.777	123.267
234	132	145	121	234	123.080	123.929	125.763
235	121	134	123	235	128.593	128.525	130.016

236	98	116	101	236	111.855	112.704	114.538
237	127	132	126	237	121.942	122.791	124.625
238	139	152	152	238	128.971	128.903	130.394
239	108	125	110	239	127.878	127.810	129.301
240	126	119	119	240	124.050	123.982	125.473
241	144	148	147	241	128.151	128.083	129.574
242	136	155	146	242	130.065	129.997	131.488
243	145	123	119	243	120.604	121.453	123.287
244	123	136	111	244	124.870	124.802	126.293
245	153	163	142	245	147.731	147.663	149.154
246	116	107	117	246	118.143	118.992	120.826
247	131	125	112	247	131.874	131.806	133.297
248	123	122	138	248	130.446	131.295	133.129
249	141	155	144	249	135.683	135.615	137.106
250	135	130	130	250	129.245	129.177	130.668
251	110	114	118	251	114.589	115.438	117.272
252	118	125	138	252	122.391	122.323	123.814
253	148	138	142	253	127.604	127.536	129.027
254	154	135	163	254	139.360	139.292	140.783
255	130	129	139	255	132.252	132.184	133.675
256	115	111	132	256	122.683	122.615	124.106
257	120	117	121	257	120.028	120.877	122.711
258	117	137	135	258	120.317	121.166	123.000
259	134	120	140	259	135.788	135.720	137.211
260	104	100	104	260	113.769	114.618	116.452
261	104	103	105	261	121.043	120.975	122.466
262	115	112	109	262	123.884	124.733	126.568
263	139	130	140	263	134.986	134.918	136.409
264	127	132	.	264	131.432	131.364	131.675
265	124	133	138	265	117.596	118.445	120.279
266	127	116	122	266	133.054	132.986	134.477
267	125	123	131	267	122.136	122.068	123.559
268	122	136	132	268	121.845	121.777	123.267
269	125	136	132	269	122.665	122.597	124.088
270	127	132	150	270	132.331	133.180	135.014
271	134	119	121	271	125.946	125.877	127.368
272	137	137	139	272	132.525	132.457	133.948
273	124	131	124	273	125.251	126.100	127.935
274	121	124	113	274	126.511	126.443	127.934
275	137	146	137	275	137.554	138.403	140.237
276	124	127	126	276	133.469	134.318	136.152
277	146	148	139	277	137.799	138.648	140.482
278	120	123	123	278	132.799	132.731	134.222
279	140	127	153	279	144.008	143.940	145.431
280	126	106	131	280	122.762	123.611	125.445
281	110	112	122	281	120.330	121.179	123.013
282	146	154	133	282	131.159	131.090	132.581
283	121	113	106	283	120.877	121.726	123.560
284	139	132	144	284	126.766	126.698	128.189
285	139	123	143	285	125.946	125.877	127.368
286	118	123	123	286	132.360	133.209	135.043
287	143	125	139	287	139.889	139.821	141.312
288	128	100	148	288	125.417	125.349	126.840
289	113	103	121	289	125.417	125.349	126.840
290	120	126	122	290	133.892	133.824	135.315
291	113	129	126	291	120.204	120.136	121.627
292	105	114	121	292	107.481	108.330	110.164
293	116	118	124	293	130.885	130.817	132.308
294	103	101	105	294	111.552	112.402	114.236
295	116	120	126	295	115.653	116.502	118.337

296	125	136	132	296	124.167	124.099	125.590
297	126	123	116	297	126.227	127.076	128.910
298	128	113	113	298	109.852	110.701	112.535
299	125	128	143	299	128.628	128.560	130.051
300	130	126	129	300	126.803	127.652	129.486
301	138	129	131	301	119.135	119.984	121.818
302	128	120	.	302	132.350	132.282	128.602
303	147	146	129	303	135.463	135.395	136.886
304	120	118	131	304	118.257	118.189	119.680
305	153	140	141	305	136.028	135.960	137.451
306	129	117	117	306	141.372	141.304	142.795
307	123	121	115	307	121.433	121.365	122.856
308	129	112	126	308	130.833	130.765	132.256
309	138	120	118	309	125.365	125.297	126.788
310	113	120	122	310	124.342	125.191	127.025
311	118	113	101	311	110.126	110.975	112.809
312	128	.	.	312	128.796	128.369	129.860
313	110	104	113	313	123.875	123.807	125.298
314	129	125	141	314	127.534	127.466	128.957
315	116	122	118	315	118.025	118.874	120.708
316	101	113	114	316	119.077	119.009	120.500
317	114	112	122	317	119.246	119.178	120.669
318	125	157	126	318	134.114	134.046	135.537
319	128	131	109	319	115.594	116.443	118.277
320	133	116	126	320	137.668	137.600	139.091
321	111	109	119	321	109.852	110.701	112.535
322	108	102	119	322	112.039	112.888	114.723
323	119	137	123	323	134.829	134.761	136.252
324	117	109	117	324	111.753	112.602	114.436
325	125	124	115	325	119.351	119.283	120.774
326	144	152	149	326	138.110	138.042	139.533
327	115	120	113	327	115.320	116.169	118.003
328	116	122	126	328	122.399	123.249	125.083
329	119	110	120	329	125.620	125.552	127.043
330	138	131	151	330	125.912	125.844	127.335
331	125	118	110	331	124.272	124.204	125.695
332	137	146	158	332	141.496	141.428	142.919
333	145	139	143	333	130.815	130.747	132.238
334	117	122	.	334	119.392	120.241	121.916
335	109	104	115	335	123.220	124.069	125.903
336	136	139	139	336	136.848	136.780	138.271
337	107	108	116	337	123.522	124.371	126.205
338	135	154	114	338	126.987	126.919	128.410
339	147	154	.	339	136.028	135.960	146.472
340	130	126	124	340	121.264	121.196	122.687
341	148	132	137	341	135.552	136.401	138.235
342	124	132	120	342	124.527	124.459	125.950
343	121	150	140	343	120.515	121.364	123.198
344	119	124	119	344	122.905	122.837	124.328
345	119	126	132	345	123.160	123.092	124.583
346	124	127	117	346	110.399	111.248	113.082
347	124	119	129	347	124.167	124.099	125.590
348	111	97	112	348	115.523	115.455	116.946
349	127	120	116	349	126.081	126.013	127.503
350	112	117	129	350	124.616	125.465	127.299
351	124	97	129	351	122.253	122.185	123.676
352	130	120	135	352	124.167	124.099	125.590
353	122	132	.	353	121.246	121.178	126.268
354	142	128	127	354	123.452	123.384	124.875
355	131	129	117	355	120.241	121.090	122.925

356	145	148	137	356	134.388	134.320	135.810
357	108	123	136	357	115.400	115.332	116.823
358	128	120	111	358	123.811	124.661	126.495

