JMP Start Biostatisticians' Quality Check on Analytical Results

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INTRODUCTION

The quality of summary and statistical results must be verified by biostatisticians prior to interpretation. JMP® can be used to verify summary and statistical results and save the results as Quality Control (QC) documentation. In addition, it has a user-friendly interface and powerful data visualization tools.

METHODS

JMP 10 and JMP Pro 11 are evaluated for generating non-model based descriptive statistics and model based statistical comparisons. Results are compared to original results from SAS® Enterprise Guide 5.1 (SAS EG). The advantages and disadvantages that JMP brings to the QC process will also be evaluated.

1. Descriptive Statistics

There are three efficient and convenient methods for descriptive summary statistics using either JMP 10 or JMP Pro 11, including "Summary", "Tabulate", and "Distribution".

Figure 1. Descriptive statistics using the "Tables" menu and "Tabulate" function

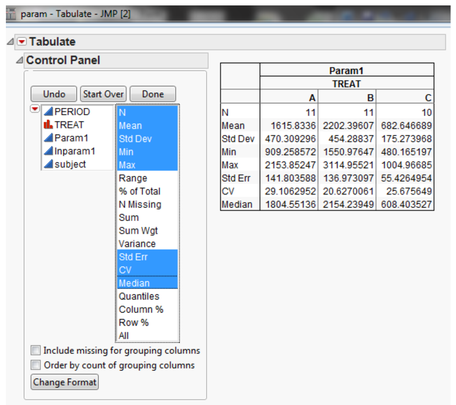


Figure 2. Descriptive summary statistics for a hypothetical pharmacokinetic (PK) parameter by PROC MEANS in SAS EG

Participant ID	Parameter 1 Treatment A	Treatment B	Treatment C
1	994	2180	867
2	1560	2170	
3	909	1850	592
4	2070	2830	863
5	2010	1880	604
6	1960	2150	613
7	1800	1910	591
8	959	1550	492
9	1860	3110	1000
10	1480	2080	480
11	2150	2490	719
N	11	11	10
AM	1616	2202	682.6
SD	470.31	454.29	175.27
ACV	29.1	20.6	25.7
Med	1805	2154	6084
Min	909	1550	480
Max	2150	3110	1000
GM	1544	2162	663.6
GCV	33.9	20.1	25.2

JMP produces descriptive statistics very efficiently with a user-friendly interactive interface. All variable names, available statistics, plots, alpha levels, and tests are available for selection. Without typing or memorizing SAS codes, summary statistics, distributional histograms, box plots, mean tests can be quickly generated to QC against original results. The point-and-click, drag-and-drop methods, and editable data table enable JMP to save some data manipulation steps. However, GM and GCV cannot be directly produced by JMP, as well as in SAS EG PROC MEANS. Natural log transformed parameter and back-transformation are needed.

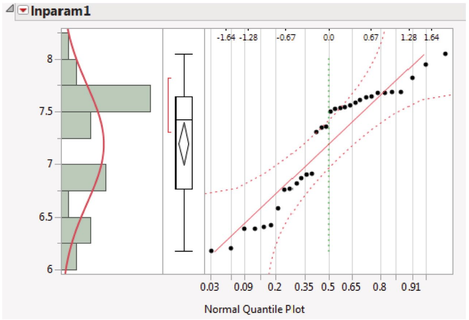
2. Data Visualization

The "Analyze" menu and "Distribution" function also provides box plots, stem and leaf plots, and normal quartile plots which can be used to examine the assumption of the underlying distribution for a parameter of interest as PROC UNIVARIATE in SAS. In addition, graphics can be produced to visualize the distribution of data from the Graph menu.

3. QC documentation

The summary results can be saved into a MS Word document, PDF file, or a data table as QC documentation. By right-clicking the summary results table, users can select the option "Make Into Data Table". Alternatively, it is possible to click the "Save as" option in the "File" menu.

Figure 3. Distribution of log transformed parameter



4. Model Based Statistics

Statistical comparisons among treatments are usually performed on PK parameters in early phase clinical studies. In the example below, treatments B and C (test), measured in Period 2 are compared against treatment A (reference) administered in Period 1 in a fixed sequence design. To account for correlation between the repeated measurements on each participant and possibility for unequal treatment variance, an unstructured variance-covariance structure is specified. The SAS EG codes are shown as in Figure 4.

Figure 4. SAS EG codes for the statistical analysis in a mixed model

```
Proc Mixed data=total;
  class Subject Treatment;
  model lnparam1 = Treatment / s ddfm=kr;
  repeated Treatment / subject = Subject type = un;
  estimate "B vs. A" Treatment -1 1 0 / cl alpha=0.1 e;
  estimate "C vs. A" Treatment -1 0 1 / cl alpha=0.1 e;
  lsmeans Treatment / cl alpha=0.05;
  lsmeans Treatment / cl alpha=0.10;
run;
```

Figure 5. Selection of a mixed model analysis for generating model based statistics in JMP

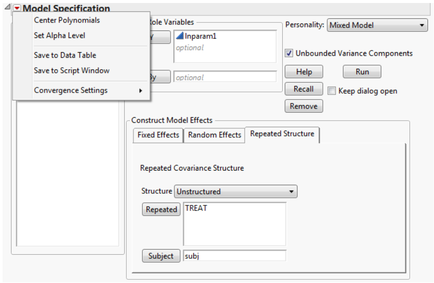


Figure 6. Comparison results from JMP

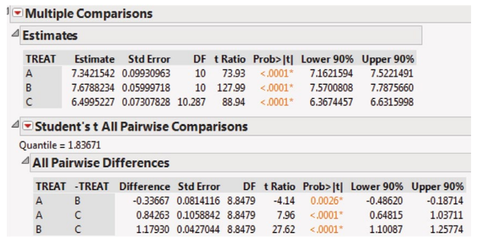


Figure 7. Comparison results from SAS EG

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
B vs. A	0.3367	0.08141	10	4.14	0.0020	0.1	0.1891	0.4842
C vs. A	-0.8426	0.1059	10.2	-7.96	<.0001	0.1	-1.0342	-0.6511

Least Squares Means

Effect	Dosage Regimen	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
TREAT	A	7.3422	0.09931	10	73.93	< .0001	0.05	7.1209	7.5634
TREAT	B	7.6788	0.06000	10	127.99	< .0001	0.05	7.5451	7.8125
TREAT	C	6.4995	0.07308	10.3	88.94	< .0001	0.05	6.3373	6.6617
TREAT	A	7.3422	0.09931	10	73.93	< .0001	0.1	7.1622	7.5221
TREAT	B	7.6788	0.06000	10	127.99	< .0001	0.1	7.5701	7.7876
TREAT	C	6.4995	0.07308	10.3	88.94	< .0001	0.1	6.3674	6.6316

RESULTS AND CONCLUSION

- Least squares means, standard errors and associated confidence intervals (CIs) are identical between the two software packages (Figures 6 and 7).
- With JMP it is not possible to write the estimate statements needed to calculate the desired treatment differences. Therefore, an all-means-comparison procedure using "Student's t" was used to calculate the mean differences and associated CIs. This provides no control over how the difference is calculated. Thus, in this example, the sign on the difference and CIs is the opposite of that generated using the SAS estimate statements.
- The inability to write estimate statements would prevent the use of JMP Pro 11 for the assessment of steady state.
- JMP Pro 11 has a "mixed models" option to model repeated measures Analysis of Variance (ANOVA), whereas other versions of JMP do not. Although several variance-covariance structures are available in JMP Pro 11, the selection is limited. If the desired statistical analysis is beyond the capabilities of JMP Pro 11, the analysis can be submitted to SAS for more complex analyses.
- The Kenward-Roger's adjustment for the denominator degrees-of-freedom is the default method.
- Alpha level is defaulted to 0.05. The Alpha level can be changed 0.1 for the whole analysis, but it cannot be specified for just a specific set of comparisons.
- The interactive user-friendly interface is very efficient. In addition, powerful graphing tools can be used for data exploration.