Paper 217-26

Clinical Trial System - A Front End SAS/AF® Application

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ABSTRACT

The procedure of clinical trial is becoming more and more standardized, especially when prepared for NDA submission, that makes it possible to build a commonly used system to perform the routine and standard data analyses. SAS® System almost dominates the pharmaceutical and clinical trial research industry. However, with the stiff study curve, it's hard to comprehend such a powerful but complicated tool. Building a front end computer system to perform the standard data analyses should be considered for several reasons:

1. Convenience
2. Reduce training time and cost. Users don't need to be SAS professionals.
3. Reduce programming time and increase productivity
4. A quick tool for QC/QA
5. Produce quick reports to management groups

With the powerful features of SAS System, especially SAS/AF, such a front end system became feasible. This paper is to introduce some ideas to build a front end system based on the standard clinical research procedure. An example - Clinical Trial System will be presented.

INTRODUCTION

Clinical Trial System(the System) was designed for clinical trial research. It was built using SAS/AF. It works for SAS 6.12 or higher versions on Windows. The System has three main parts:

1. Data Management
2. Data Analysis
3. Internet Application

It has simplified the clinical trial research process. With this System, manual programming is not necessary, it can write programs for you. Also, it can convert the output tables and SAS data sets into HTML files. All users need to do is to select the data that users want to work on and click the menu icons, users don't even need to worry about the Libname and Filename definitions. It saves time and resources.

SYSTEM HIGHLIGHTS

1. DATA MANAGEMENT

Through Data Management System, you can enter, edit, manipulate, validate, view, import, export and report data.

I. Data Entry
   1. Keyboard Data Entry: Create an new data set or edit an existing data set
   2. Import Data From Data Sources : SAS transport file, Text file, Excel file, Oracle data and SPSS data
   3. Download Data From Internet

II. Data Manipulation
   1. Set data
   2. Sort data
   3. Merge data
   4. Append data
   5. Concatenate

III. Data Validation
   1. Validate data by checking data distribution
   2. Validate data by comparison to a standard data

IV Data Review
   1. Multiple data sets can be viewed in the same time.

V. Data Export
   1. Export in SAS transport format
   2. Export to DBMS - Oracle
   3. Export to MS Excel

VI. Data Report
   1. Data Structure Report: Only report data set structure without data
   2. Data Report: Report data in simple format

2. DATA ANALYSIS

Data Analysis System is featured with Descriptive Analysis, Safety Analysis (Prior/Concurrent Medication, Vital Sign, Adverse Events and Laboratory Test), ANOVA Analysis, Pairwise Comparison, Survival Analysis and Graphic Analysis. It can generate output files in text format, HTML and PDF format. Graphic output can also be converted into Postscript, CGM and GIF format.

I. Descriptive Analysis
   Descriptive Analysis System is designed for basic statistical analysis, it can be used for summary analysis. For example:
   1. Demographic Information Summary
   2. Study Termination Reason Summary,
   3. … … etc.

II. Incidence Summary
   Incidence Summary System includes: Prior/Concurrent Medication Use Analysis, Prior/Concurrent Surgical Procedure Analysis, Medical History Analysis and other Incidence analysis. It can not only summarize the incidence but also compare the equality of proportions across different groups using CMH test.

III. Adverse Events Analysis
   It can not only summarize the incidence of Adverse Events but also compare the equality of proportions across different groups using CMH test.
   1. Summary of Adverse Event Report
   2. Incidence of Adverse Events
   3. Incidence of Adverse Events by Body System
   4. Incidence of Adverse Events by Severity
   5. Incidence of Adverse Events by Attribution
   6. Incidence of Serious Adverse Events
   7. Incidence of Adverse Events Causing Withdrawal
   8. Incidence of Adverse Events by Subgroup
   9. Frequency of Adverse Events

IV. Vital Sign Analysis
Vital sign information can be summarized through Descriptive Analysis System.

V. Laboratory Test Analysis
1. Summary of Laboratory Test
2. Summary of Laboratory Test Change
3. Lab Test Change Relative to Normal Range
4. Laboratory Test Distribution Among Ranges
5. Laboratory Test Shift Plot

VI. ANOVA Analysis
ANOVA p-values can be calculated using GLM model.

VII. Pairwise Comparison Analysis
Pairwise comparison p-values can be calculated using GLM Model.

VIII. Survival Analysis
Proportion of survival can be estimated and the results will be presented in graphic format.

IX. Graphic Analysis
Data can be summarized and visually displayed using plot, joint line, smooth line, regression line, pie, bar or block. Data used to generate the graphs can also be displayed on the graphs for review.

X. Data Listing

3. INTERNET APPLICATION

Internet Application provides an easy way to read information from Web, convert SAS data sets into HTML format and connect to the Web site you like.

4. PROGRAM WINDOW

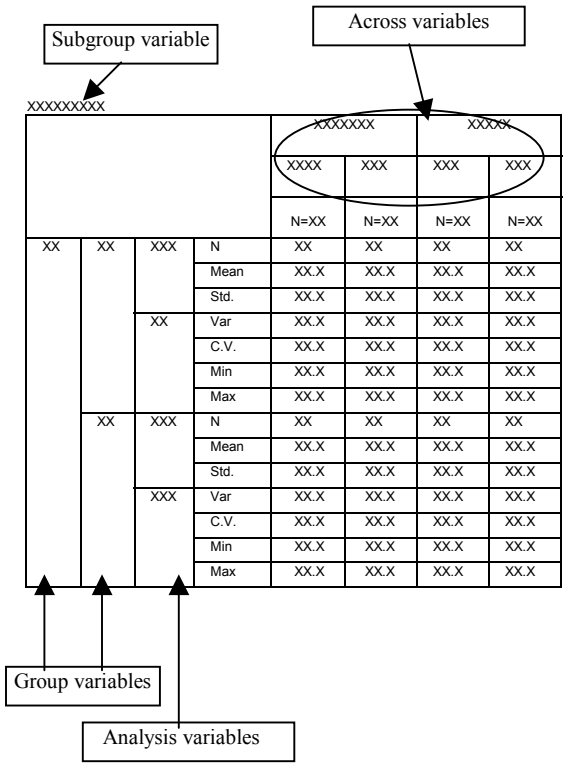
For each data analysis output, the System creates a program for it. Through the program window, the program can be recalled and saved for future use.

A SAMPLE OF DATA ANALYSIS OUTPUTS

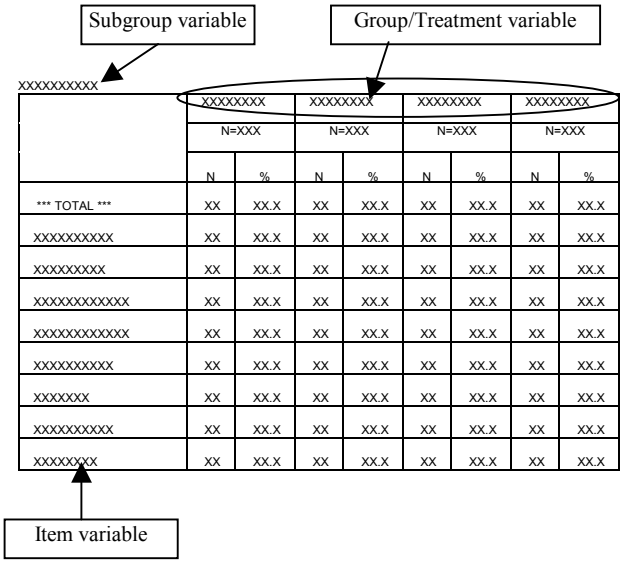
Descriptive analysis can be used to calculate the following statistics:

N, Percent, Mean, Standard Deviation, Standard Error, Variance, C.V., Median, Q1, Q3, Qrange(Q3 – Q1), P5, P95, Minimum, Maximum, Range,

Descriptive Analysis



Summary of Prior/Concurrent Medication Use (1)
(Summary of Prior/Concurrent Surgical Procedure)



Summary of Prior/Concurrent Medication Use (2)
(Summary of Prior/Concurrent Surgical Procedure)

XXXXXXXXXX

	XXXXXXXX N=XXX		XXXXXXXX N=XXX		XXXXXXXX N=XXX		
	N	%	N	%	N	%	P-value
*** TOTAL ***	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX

Summary of Adverse Events Report

XXXXXXX

	XXXXX N=XX		XXXXX N=XX		XXXX N=XX	
	N	%	N	%	N	%
Subject Reporting AE	XX	XX.X	XX	XX.X	XX	XX.X
Subject Reporting AE By Attribution - Possible	XX	XX.X	XX	XX.X	XX	XX.X
Subject Reporting AE By Attribution - Probable	XX	XX.X	XX	XX.X	XX	XX.X
Subject Reporting AE By Attribution - Definite	XX	XX.X	XX	XX.X	XX	XX.X
Subject Reporting AE By Severity - Mild	XX	XX.X	XX	XX.X	XX	XX.X
Subject Reporting AE By Severity - Moderate	XX	XX.X	XX	XX.X	XX	XX.X
Subject Reporting AE By Severity - Severe	XX	XX.X	XX	XX.X	XX	XX.X
Subject Reporting Serious AE - Non-fatal	XX	XX.X	XX	XX.X	XX	XX.X
Subject Withdrawn Due to AE	XX	XX.X	XX	XX.X	XX	XX.X
Number of Deaths	XX	XX.X	XX	XX.X	XX	XX.X

Incidence of Adverse Events (1)
(Incidence of Serious Adverse Events)
(Incidence of Adverse Events Causing Withdrawal)

XXXXXXXXXX

ADVERSE EVENTS	XXXXXXXX N=XXX		XXXXXXXX N=XXX		XXXXXXXX N=XXX		XXXXXXXX N=XXX	
	N	%	N	%	N	%	N	%
*** TOTAL ***	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
XXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
XXXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
XXXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
XXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
XXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X

Incidence of Adverse Events (2)
(Incidence of Serious Adverse Events)
(Incidence of Adverse Events Causing Withdrawal)

XXXXXXXXXX

ADVERSE EVENTS	XXXXXXXX N=XXX		XXXXXXXX N=XXX		XXXXXXXX N=XXX		
	N	%	N	%	N	%	P-value
*** TOTAL ***	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX
XXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X	X.XXX

Incidence of Adverse Events by Body System (1)
(Incidence of Serious AE by Body System)
(Incidence of AE Causing Withdrawal by Body System)

XXXXXXXXXX

BODY SYSTEM / ADVERSE EVENTS		XXXXXXXX N=XXX		XXXXXXXX N=XXX		XXXXXXXX N=XXX	
		N	%	N	%	N	%
XXXXX	*** TOTAL ***	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
XXXX	*** TOTAL ***	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X

Incidence of Adverse Events by Body System (2)
(Incidence of Serious AE by Body System)
(Incidence of AE Causing Withdrawal by Body System)

XXXXXXXXXX

BODY SYSTEM / ADVERSE EVENTS		XXXXXXXX N=XXX		XXXXXXXX N=XXX		
		N	%	N	%	P-value
XXXXX	*** TOTAL ***	XX	XX.X	XX	XX.X	X.XXX
	XXXXXXXXXXX	XX	XX.X	XX	XX.X	X.XXX
	XXXXXXXXXXX	XX	XX.X	XX	XX.X	X.XXX
	XXXXXXXXXX	XX	XX.X	XX	XX.X	X.XXX
XXXX	*** TOTAL ***	XX	XX.X	XX	XX.X	X.XXX
	XXXXXXXXXX	XX	XX.X	XX	XX.X	X.XXX
	XXXXXXXXXX	XX	XX.X	XX	XX.X	X.XXX
	XXXXXXXX	XX	XX.X	XX	XX.X	X.XXX
	XXXXXXXXXX	XX	XX.X	XX	XX.X	X.XXX

Incidence of Adverse Events by Severity

XXXXXXXXXX

BODY SYSTEM / ADVERSE EVENTS		XXXXXXXXXXXXXXXXX N=XXX					
		Mild		Moderate		Severe	
		N	%	N	%	N	%
XXXXXX	*** TOTAL ***	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
XXXX	*** TOTAL ***	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X

Incidence of Adverse Events by Attribution

XXXXXXXXXX

BODY SYSTEM / ADVERSE EVENTS		XXXXXXXXXXXXXXXXX N=XXX					
		Possible		Probable		Definite	
		N	%	N	%	N	%
XXXXXX	*** TOTAL ***	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
XXXX	*** TOTAL ***	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X
	XXXXXXXXXX	XX	XX.X	XX	XX.X	XX	XX.X

Lab Test Change Relative to Normal Range

XXXXXXXXXXXX

LAB TEST		XXXXXXXXX		XXXXXXXXX		XXXXXXXXX	
		N	%	N	%	N	%
XXXXXXXXX	Decrease	XX	XX.X	XX	XX.X	XX	XX.X
	Increase	XX	XX.X	XX	XX.X	XX	XX.X
	No change	XX	XX.X	XX	XX.X	XX	XX.X
	Total	XX	XX.X	XX	XX.X	XX	XX.X
XXXXX	Decrease	XX	XX.X	XX	XX.X	XX	XX.X
	Increase	XX	XX.X	XX	XX.X	XX	XX.X
	No change	XX	XX.X	XX	XX.X	XX	XX.X
	Total	XX	XX.X	XX	XX.X	XX	XX.X
XXXXXX	Decrease	XX	XX.X	XX	XX.X	XX	XX.X
	Increase	XX	XX.X	XX	XX.X	XX	XX.X
	No change	XX	XX.X	XX	XX.X	XX	XX.X
	Total	XX	XX.X	XX	XX.X	XX	XX.X

Lab Test Distribution Among Ranges

LAB TEST = XXXXX

XXXXXX1

(N)	H	L	N	TOTAL
H	3	0	0	3
L	0	4	0	4
N	0	1	73	74
TOTAL	3	5	73	81

<PRE-TIME> POSTTIME

XXXXXX2

(N)	H	L	N	TOTAL
H	2	0	1	3
L	0	4	2	6
N	1	1	68	70
TOTAL	3	5	71	79

<PRE-TIME> POSTTIME

XXXXXX1

(%)	H	L	N	TOTAL
H	3.7	0	0	3.7
L	0	4.9	0	4.9
N	0	1.2	90.1	91.4
TOTAL	3.7	6.2	90.1	100.0

<PRE-TIME> POSTTIME

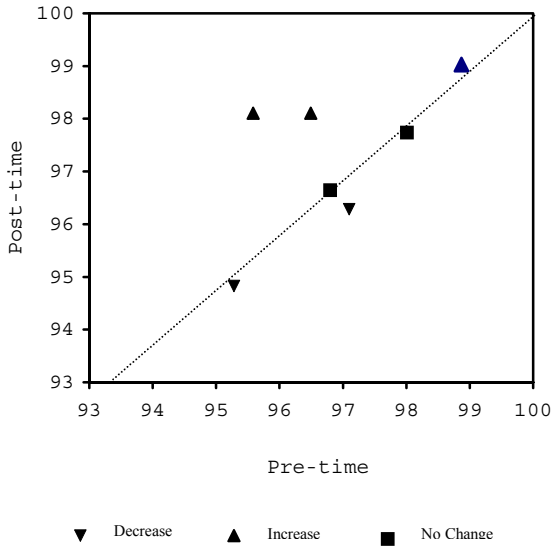
XXXXXX2

(%)	H	L	N	TOTAL
H	2.5	0	1.3	3.8
L	0	5.1	2.5	7.6
N	1.3	1.3	86.1	88.6
TOTAL	3.8	6.3	89.9	100.0

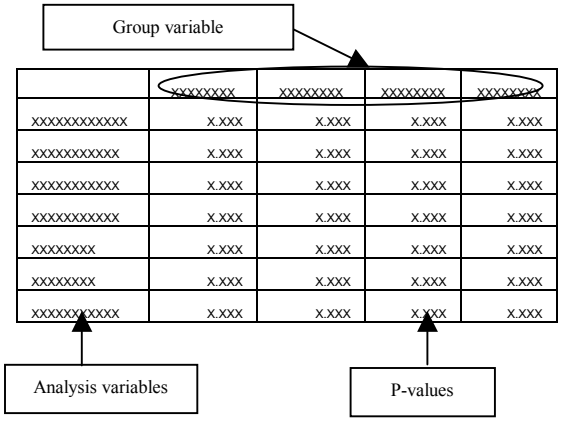
<PRE-TIME> POSTTIME

Lab Shift Plot

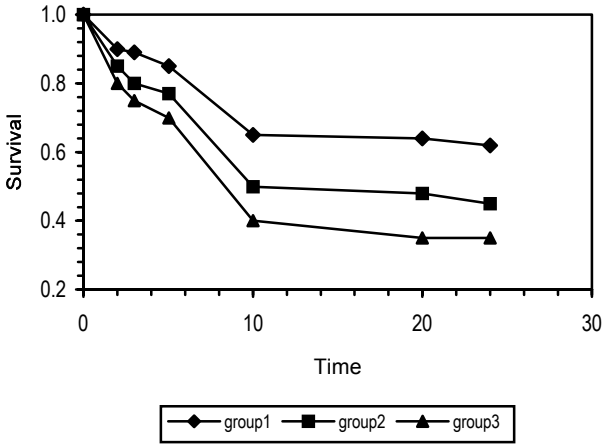
LAB TEST= XXXX, TREATMENT=XXXX (N=XXX)



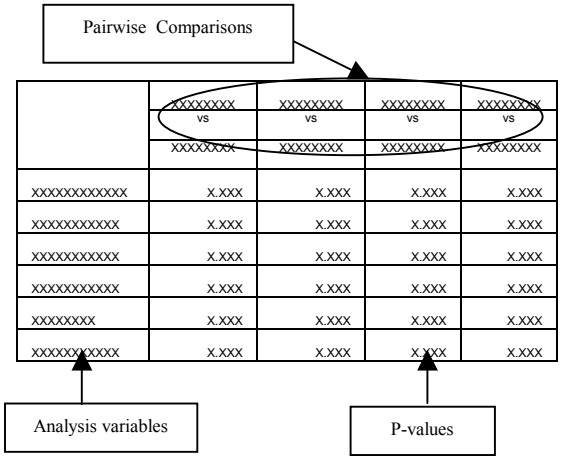
ANOVA Analysis



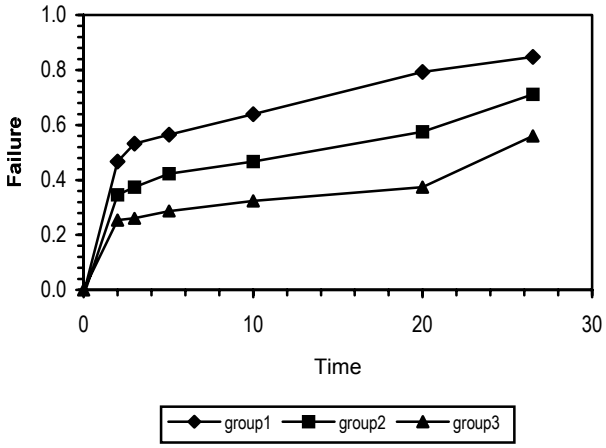
Survival Analysis – Plot of Survival



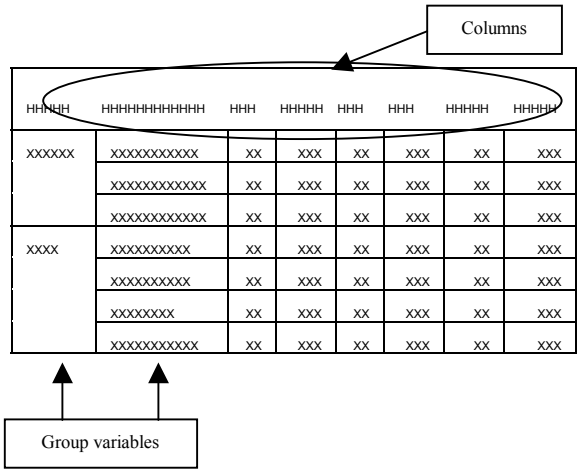
Pairwise Comparison Analysis



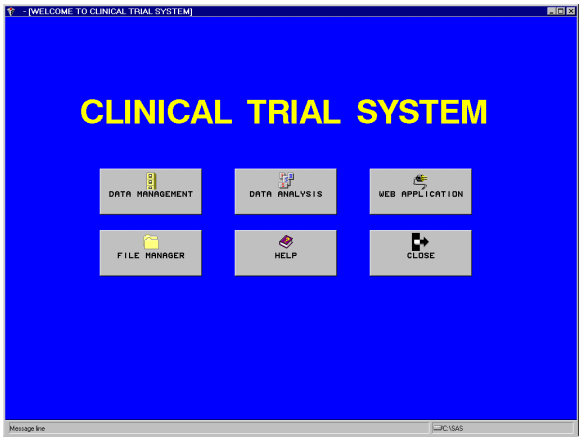
Survival Analysis – Plot of Failure



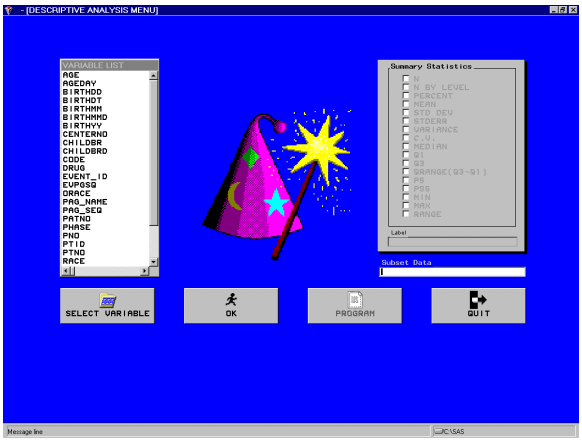
Data Listing



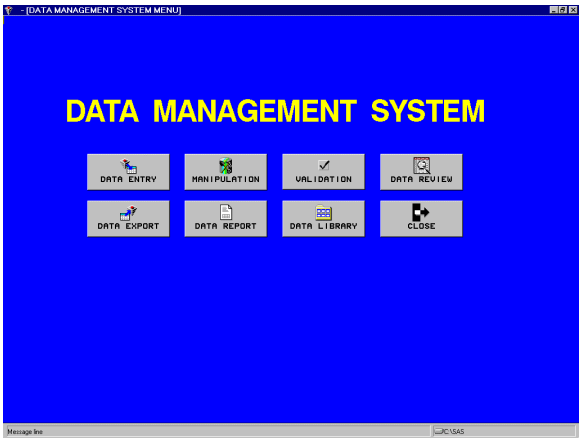
A SAMPLE OF SYSTEM SCREENS



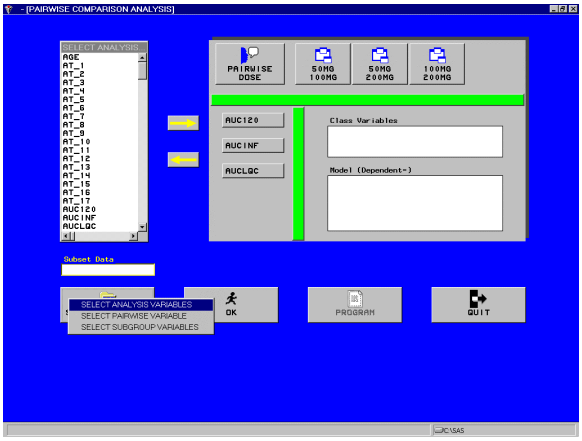
This is the 'Welcome Screen' from where Data Management Screen, Data Analysis Screen and Web Application Screen can be accessed.



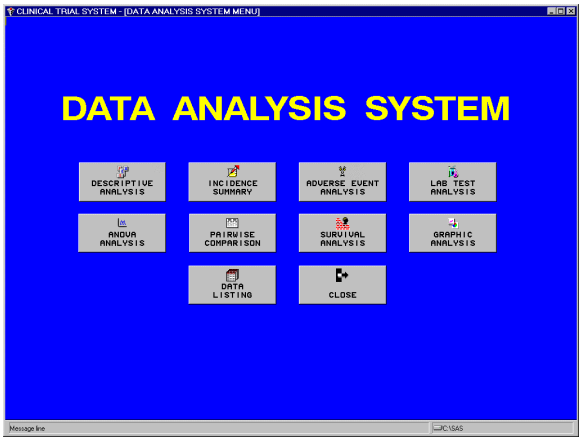
Descriptive Analysis Screen has the flexibility to do all summary analyses. All users need to do is just a click to the button to select the data and the variables users want to use.



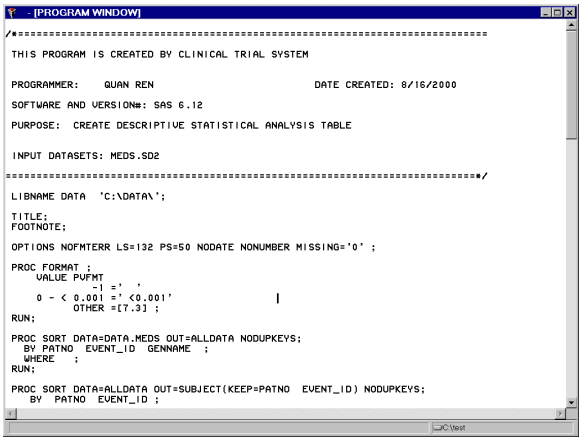
Data Management Screen has access to all data manipulation features.



Pairwise comparison using GLM model has been simplified. Complicated p-value calculation procedure became a simple menu system.



Data Analysis Screen includes all data analysis menu including data listing menu.



Click the PROGRAM button on each individual analysis screen, the analysis program will be opened in PROGRAM WINDOW where users can modify and save the program.

CONCLUSIONS

This paper highlighted the Clinical Trial System, there are still a lot of other features not mentioned. For instance, the File Manager which can run existing SAS programs, write or edit a text file and Copy or Rename a file. Although this System includes a lot of standard data manipulation or analysis methods, there are still some other methods which need to be considered. For example, T-test and Contrast analyses. Even so, the System is still a quick and convenient tool. It can be easily shipped and installed on your site. It can run on your SAS System without SAS/AF module installed on your site.

TRADEMARKS

REFERENCES

SAS Institute Inc. (1990), *SAS Language: Reference, Version 6, First Edition*, Cary, NC: SAS Institute Inc.

SAS Institute Inc. (1993), *SAS/AF Software: FRAME Entry Usage and Reference, Version 6, First Edition*, Cary, NC: SAS Institute Inc.

CONTACT INFORMATION

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