STATISTICS AUTOMATION: USING SAS MACROS TO PRODUCE REPORT-READY STATISTICAL ANALYSIS TABLES

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Abstract

Experimental designs are often similar or identical to designs of studies previously analyzed. For example, in large-scale clinical trials, analyses of individual centers or other subgroups of patients are often required. For this reason, SAS macros have been written to analyze data. These are general in the sense that they can be readily re-applied to a later study with the same basic design.

The macros require only that the SAS dataset be in a specified conventional form, and that several parameters be defined prior to invoking them. Hence, they are quite simple to use. The output is a statistical table, complete with summary statistics, tests of hypotheses, and confidence intervals. These tables are suitable for direct insertion into statistical reports.

The purpose of this paper is to familiarize the reader with the technique of writing these macros, and to point out the advantages the macros offer. A relatively simple macro is presented as a demonstration of the technique. Additionally, output from a relatively complex nonparametric analysis is presented to illustrate the usefulness of the technique. This latter macro has been used repeatedly by the author to analyze efficacy data and laboratory data from studies of anti-depressive and anti-inflammatory compounds.

1. Motivation for Writing General Macros

The job of a statistician in medical applications often requires that a statistical report be written. This report usually includes summary tables. The entire process of preparing statistical reports can be facilitated by writing SAS macros which produce report-ready analysis tables.

Typically, statisticians analyzing a set of data find themselves having to do a number of tasks in the process:

1. Rearrange or manipulate the dataset.
2. Use several existing SAS procedures, each performing only a part of the total analysis.
3. Write their own SAS code to perform an analysis, or part of an analysis, for which a SAS procedure does not exist.
4. Then, by hand, copy descriptive statistics, p-values, etc., from various locations of the output onto sheets of paper, have the table typed, and then check it back to the original computer printout.

These 4 steps are further confounded by having several variables which are subjected to the statistical analysis, rather than only one. Also, if errors in the data are discovered after the tables have been typed and checked, one may need to go through step 4 more than once.

Many of these steps can be averted in future studies with designs similar to the present experimental design by initially writing general SAS macros. It greatly simplifies the process of analysis in the long-term. Subjecting numerous variables to analysis takes no more effort than a single variable, as will become evident in subsequent sections. And, if errors in the data are found after generating the statistical tables, all that is required is to rerun the program.

Approximately 20 different macros have been written to date. Although they are specific to clinical trials, the method can be useful to any area where particular study designs are routinely used. The macros are continually being added to and modified by the author, so it was not feasible to list them here. Nor was it feasible to offer a listing or tape of the macros upon request. Rather, the objective of this paper is to demonstrate the usefulness of writing general SAS macros, and to outline a method to do so.

2. Use of Macros

This section describes the kinds of parameters which need to be defined prior to invoking the macros. Essentially, anything which may be different between two similar study designs (e.g. the variables analyzed) must be defined in a sub-macro, PROC FORMAT, or LABEL statement. These are then called or referenced in one or more locations of the large macro.

Firstly, the dataset must be in a specified conventional form prior to invoking the macros. The dataset typically must include 3 to 5 variables with specific names. These are variables such as PATIENT (patient number), DRUG (treatment groups), or VISIT (study visit number).

Several sub-macros also must be defined. Typically, they contain:
1. A list of the variables to be analyzed.
2. The titles to be printed on the tables.
3. Specification of the format(s) to be used for the descriptive statistics (i.e. how many decimal places).
4. Designation of a one-tailed or two-tailed test.
5. A sub-macro which allows for suppression of portions of the table (e.g. p-values).
A PROC FORMAT statement is usually required, providing names for the treatment groups. Labels are printed in place of the variable names when they are specified in a data step with a LABEL statement.

All necessary sub-macros are usually only one or two lines long. Consequently, statistical analysis using an existing SAS macro is simple and straightforward. The program needed to invoke the macro is often only 20 lines or less.

3. Technique for Writing Macros

This section outlines the way in which the macros are organized. Similarities amongst the macros simplify their creation and usage. Basically, the macro first transposes the dataset so that a separate observation exists for each patient-visit-variable. In the process, a variable called VARIABLE is created, with values 1, 2, ..., where the number corresponds to the position that the variable name appears in the variable list (defined by a sub-macro called _VAR).

Next, the analyses are conducted. This may include several SAS procedures, or a block of SAS code that performs an analysis for which a SAS procedure does not exist (e.g. construction of confidence intervals). The SAS procedure PRINTTO is often employed in the macros to output portions of the ANOVA table from PROC GLM. The results from these various analyses are output to datasets, and merged into a single dataset prior to printing the tables.

Finally, the tables are printed using "PUT" statements, using standard report-writing techniques available in SAS.

As already mentioned, the author has written numerous macros for applications in clinical studies. In each case, any number of variables can be analyzed. These macros include:

1. Several macros which print means, standard deviations, and sample sizes in each of two treatment groups, across time.
2. Nonparametric analyses (Wilcoxon Rank Sum and Wilcoxon Signed Rank tests), with two or three treatment groups.
3. Analysis of variance, with one covariate.
4. Analysis of variance on the ranks, with one or two covariates.
5. Analysis of variance for a crossover design.

Many of these include confidence intervals in addition to tests of hypotheses.

4. A Front-End User-Friendly System

Recently, the author developed a user-friendly front-end to the macros, using PROC FSEDIT. This system has evolved greatly with the help of several colleagues at Lilly Research Laboratories.

The system allows the user to simply type a key word (such as "MACRO") after logging onto TSO, which calls a pre-defined CLIST that automatically brings up a FSEDIT screen.

The first screen contains, among other job JCL parameters, options that identify available analyses. For example, choice of an option answers questions such as (i) are there two or three treatment groups, (ii) is the design parallel or crossover, (iii) is a parametric or nonparametric analysis desired, or (iv) are there any covariates to be included in the analysis. Choosing an option brings up a particular set of screens (also using PROC FSEDIT). These screens contain blanks that the user must fill in with information necessary for the particular macro.

This FSEDIT is being performed on a dataset with one observation. The variables relate to the sub-macros and other information needed to invoke the macro. This interactive procedure is essentially a program generator. After the screens have been filled out, the user pushes a button which writes the program and submits a batch job. The end result is computer-generated statistical analysis tables which can be directly included into a report. A printer with quality printout like the Xerox 9700 is ideal for this purpose.

With this front-end system, analyzing a set of data is greatly simplified. In fact, the user of this user-friendly system does not even need to know how to program SAS. See Hardison and Muller (1984) for a detailed description on the use of PROC FSEDIT to generate SAS code. Other applications of this interactive technique are discussed in Enas, Hardison, and Rockhold (1984) and Muller (1984).

5. Example 1

This first example consists of a relatively simple macro. It has a very limited applicability, as will be seen below. However, it is easy to follow and illustrates the technique of creating the macros.
This macro creates a table containing means, standard deviations, and sample sizes in each of two treatment groups. These descriptive statistics are presented in the table for each of weeks -1 through 6, a total of 8 weekly measurements. This macro is appropriate for a 7-week study where data are collected at weekly intervals, beginning at one week prior to active drug (week -1). The output contains up to three variables on a single page.

The macro is listed below:

```
MACRO MN8WEEK
DATA FORMATS; SET WOWO:
LENGTH LLABELS $ 40; ARRAY X VAR' KEEP LABELS:
IF N-1 THEN DO OVER X; CALL--LABEL X.LLABELS; OUTPUT; END.
ELSE STOP;
DATA ANALYSIS; SET WOWO; DROP _VAR:
ARRAY LIST (VARIABLE) VAR; RUN:
PROC SORT: BY VARIABLE DRUG WEEK;
PROC MEANS NOPRINT MEAN STD N: BY VARIABLE DRUG WEEK;
VAR RESPONSE;
OUTPUT OUT=PRJNT MAN-MAN STD N:
DATA PRINT; SET PRINT; BY VARIABLE DRUG;
IF N=O THEN N=.; JF FIRST DRUG THEN VISIT=O; VISIT .. I:
DATA NULL; SET PRINT ENO=EOF; FILE PRINT N=PAGESIZE:
BY VARIABLE DRUG: RETAIN LINE -7:
IF FIRST.VARIABLE AND FIRST.DRUG Then LINE-4 CDL o 33 + (VISIT-I)*12;
IF FIRST.DRUG Then PUT RUNE I II II " DRUG __ DRUG.
PUT NLINE III @COL MEAN @>COL STD FORMAT III @>COL N 11-:-;
RETURN;
HEADER: llNE"S;
IF LINE=2 THEN PUT I(0)7 124*'-'
I ~(K'1:31 ':'
I ~(6 '21'MEAN'@l13l ':,'
I ~(0'6 ,I, (QI2S 'STD' @131 ':
I ~(6 ,I, ;;>30 'N' (iil131 ':'
W6 ,I, ;;>30 'N' @13l ':'
~6 ,I, ;;>30 'N' :'
"5 ,I, (!P131 5
~6 ,I, 1§'27
CDL o 33 +
RETURN;
FORMAT VARIABLE LLABELS_ DRUG __ DRUG.; TITLE
This program is relatively short; not much information has to be passed to the macro. Macro _VAR contains the names of the variables to be analyzed. Macro _FORMAT contains the format to be used for the means and standard deviations in the table. It must be of length 12, but any number of decimal places can be specified. Macro _TITLE contains the titles to appear on the tables. The PROC FORMAT specifies names for the treatment groups (maximum length is 18). The dataset that is passed to the macro must be called "WOWO". Finally, the statement _MN8WEEK executes the macro.

Finally, the output for a single variable is presented below:

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>WEEK -1</th>
<th>WEEK 0</th>
<th>WEEK 1</th>
<th>WEEK 2</th>
<th>WEEK 3</th>
<th>WEEK 4</th>
<th>WEEK 5</th>
<th>WEEK 6</th>
<th>WEEK 7</th>
<th>WEEK 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment 1</td>
<td>MEAN</td>
<td>30.13</td>
<td>31.58</td>
<td>31.29</td>
<td>18.06</td>
<td>19.79</td>
<td>12.57</td>
<td>11.09</td>
<td>9.35</td>
<td>6.31</td>
</tr>
<tr>
<td>N</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td>N</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
</tr>
</tbody>
</table>

Descriptive Statistic
Macro MN8WEEK

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The output presented above corresponds to one variable. Each page of the table would contain up to three variables. In practice, the labels for the variables and the names for the treatment groups would be more informative than the example presented here.

6. Example 2

This is a nonparametric analysis of a clinical study involving 3 investigators (locations), with 2 drug groups. This macro required only 20 lines of SAS code for execution. The macro itself is approximately 440 lines, including a few lines of documentation.

The printout for one of the variables is presented at the bottom of this page.

A great deal of information about a single variable is contained on this single page of output. First of all, analyses of variance are performed on the ranks at baseline (prior to study drug administration), and on the difference of baseline minus post-therapy. "Post-therapy" can be defined by the user as endpoint (last visit at which a particular measurement was obtained), a fixed visit, or the average of all visits after study drug therapy was commenced.

The ANOVA at baseline is presented at the top left of the table. The ANOVA for the difference is at the top right. The model consists of the effects due to investigator, drug group, and their interaction. The ANOVA tables contain the degrees of freedom (DF), mean square (MS), F-statistic (F), and significance level (PROB) for each effect in the model. Degrees of freedom and mean square for error are also included.

Nonparametric Analysis of Studies with Two Treatment Groups
Macro NCD1

VARIABLE: VARIABLE #1

ANALYSIS OF VARIANCE ON RANKS

<table>
<thead>
<tr>
<th>SOURCE</th>
<th>BASELINE</th>
<th>DIFFERENCE (BASELINE - THERAPY)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DF</td>
<td>MS</td>
</tr>
<tr>
<td>Investigator (Pl)</td>
<td>2</td>
<td>22315.62</td>
</tr>
<tr>
<td>DRUG</td>
<td>2</td>
<td>3980.50</td>
</tr>
<tr>
<td>DRUG*DRUG</td>
<td>3</td>
<td>316.80</td>
</tr>
<tr>
<td>ERROR</td>
<td>111</td>
<td>759.15</td>
</tr>
</tbody>
</table>

DESCRIPTIVE STATISTICS AND NONPARAMETRIC ANALYSIS (UNADJUSTED FOR PROGNOSTIC PARAMETERS)

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>N</th>
<th>MEAN</th>
<th>STD PRBB</th>
<th>MINIMUM</th>
<th>MAXIMUM</th>
<th>MEDIAN</th>
<th>MEAN RANK COMPARISON</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASELINE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment #1</td>
<td>60</td>
<td>31.60</td>
<td>7.42</td>
<td>0.00</td>
<td>84.00</td>
<td>33.50</td>
<td>65.62</td>
</tr>
<tr>
<td>Treatment #2</td>
<td>57</td>
<td>20.37</td>
<td>7.19</td>
<td>18.00</td>
<td>50.00</td>
<td>19.00</td>
<td>54.24</td>
</tr>
<tr>
<td>POST- THERAPY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment #1</td>
<td>60</td>
<td>14.64</td>
<td>11.99</td>
<td>0.00</td>
<td>49.00</td>
<td>10.00</td>
<td>27.58</td>
</tr>
<tr>
<td>Treatment #2</td>
<td>57</td>
<td>17.21</td>
<td>12.16</td>
<td>0.00</td>
<td>47.00</td>
<td>16.00</td>
<td>24.52</td>
</tr>
<tr>
<td>DIFFERENCE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment #1</td>
<td>60</td>
<td>18.73</td>
<td>12.33</td>
<td>&lt;.001</td>
<td>18.00</td>
<td>18.50</td>
<td>64.24</td>
</tr>
<tr>
<td>Treatment #2</td>
<td>57</td>
<td>15.98</td>
<td>12.15</td>
<td>&lt;.001</td>
<td>10.00</td>
<td>11.00</td>
<td>63.48</td>
</tr>
</tbody>
</table>

95% CONFIDENCE INTERVAL ON MEAN TREATMENT DIFFERENCE: LOWER LIMIT = -1.60, UPPER LIMIT = 8.84

** TWO-TAILED WILCOXON SIGNED RANK TEST
NOTE: ALL WILCOXON RANK SUM TESTS ARE TWO-TAILED
ANOVA CONTAINS TWO-TAILED TESTS, USING THE ERROR MEAN SQUARE AS THE DENOMINATOR OF THE F-TEST

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Below the ANOVA tables are numerous descriptive statistics, plus results of two additional nonparametric procedures. These nonparametric tests consist of the Wilcoxon Signed Rank test within each of the treatment groups, and the Wilcoxon Rank Sum test to compare the treatment groups (without taking into account possible variation due to investigators). In both cases, the adjustment for ties and the continuity correction are employed. Significance levels are obtained by utilizing the asymptotic normality of the test statistics.

The descriptive statistics are presented for data obtained at baseline, post-therapy, and their difference. Reading from left to right in the table are treatment group, sample size, mean, standard deviation, Wilcoxon Signed Rank significance level (for difference only), minimum, maximum, median, mean rank, and Wilcoxon Rank Sum significance level (the latter two only for baseline and the difference from baseline).

At the bottom, 95% confidence intervals are given for the difference between the two treatment groups, with respect to the difference from baseline. This is a parametric confidence interval, computed in the standard way (using the student's t distribution, and Satterthwaite's approximation when appropriate).

As is evident from this table, the macros can be quite complex. They may include numerous descriptive statistics, and combine several statistical procedures onto a single page of output. This expedites the review of a particular variable. So, for example, if one is interested on how two drugs compare with respect to an overall pain score in rheumatoid arthritis, the pertinent information is all on a single page.

A reference source for the ANOVA on ranks is Conover and Iman (1981). Hollander and Wolfe (1973) and Lehmann (1975) contain descriptions of the Wilcoxon Signed Rank and Wilcoxon Rank Sum procedures.

6. Discussion

In summary, writing general SAS macros requires a great deal of effort up-front. However, in the long-term, they can provide great improvements in efficiency, accuracy, and productivity. Additionally, with the user-friendly front-end to accompany the macros, they can be readily used by others. In fact, SAS novices can easily use the menu-driven system. Other potential applications for these macros include the production of summary tables for adverse events in clinical trials. It could be written in a way that any "cut" of the data could be readily examined. For example, one could request adverse reaction tables for those occurring in the first week of the study, those occurring in the first two weeks, those occurring at any time, etc.

Finally, another potential application would be to have SAS construct the entire statistical report, including text and tables. One application might be some of the Phase I clinical studies routinely conducted on new drugs. Another possibility might be the analysis of drug stability studies.

One thing to remember when attempting to create such a macro facility: There is no point in time at which the system will be complete. Just as SAS Institute will continue to improve and expand the capabilities of SAS, an ideal macro facility will continue to evolve.

REFERENCES


