

Generating Multiple Parameter Reports Into Single Report Using %Do Loop And Call Symputx

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ABSTRACT

In clinical research domain, many times programmers need to generate multiple parameter reports like laboratory (lab) tests, questionnaires and many more. Let's take lab tests reports as an example. As we all know, there are multiple lab tests performed for particular study and statisticians/investigators want to see all tests' reports into single report. At first instance, it seems difficult because programmer does not know how many lab tests are performed and without exact numbers one cannot use the Loop functionality. The term "loop" describes any control structure that causes a set of programming logic to be executed iteratively for definite number of times. Using %DO loop with Call symputx, this task can be easily performed.

INTRODUCTION

A good programmer is one who is the most efficient in day-to-day programming tasks. Many times programmers are requested to create reports inclusive of analysis of several lab tests, questionnaires and so on. This task gets more difficult with large number of parameters and complexity increases with an addition of an analysis like MMRM. In clinical trial analysis, while handling longitudinal continuous data, there are very often cases that the Mixed Model Repeated Measures (MMRM) tool is used to deal with the continuous endpoints when an outcome is collected at multiple times. It is usually up to the statistician to specify the criterion for identifying the best covariance structure against the chosen model among all possible covariance structures arranged in particular order of interest, or in the way it has been specified in Statistical Analysis Plan and/or Protocol. In order to achieve this with the use of SAS, clinical programmers have to develop a program which dynamically checks the each covariance structure by order of interest, or in the way it has been specified in Statistical Analysis Plan and/or Protocol, and to produce the estimates and main effects information based on the best covariance structure selected for the given model. As an example, the change from baseline for each visit in laboratory analyte values is common analysis to compare different treatment groups using an MMRM analysis. One might think that it can be easily performed by passing Lab test variable in BY statement, but MMRM ANOVA/ANCOVA model of all lab parameters may not get converged for same variance covariance matrix and one needs to find out the best covariance structure for each lab test separately. This task can be easily performed using %DO loop with Call symputx, which has been illustrated in the following discussion.

LAB MMRM REPORTS WITH MULTIPLE LAB TESTS

Let's say we have LAB data with all required analysis variables and we need to generate reports displaying each Lab Tests' MMRM (Mixed Model Repeated Measures) data. Please refer the below first and last page of the report. Values of Laboratory Analyte (highlighted in Yellow color) and Covariance structure (highlighted in Turquoise color) in Figure-1 and 2 will be changed accordingly for different Lab Test data.

FIGURE: 1 - First Page of the report:

Analysis of Laboratory Analyte Change from Baseline - MMRM											Page	1 of 115
ITT Patients												
ABC-DE-FGHI												
Laboratory Analyte: ALBUMIN(gram/Liter)												
Visit (Week)	Drug Group	N	Mean Change	SD	LS Mean Change	SE	Within Grp p-value [a]	LS Mean Change Difference	SE	Between Grp p-value [b]	95% CI	
4 (1.0)	DrugA	90	-1.51	2.62	-1.25	0.22	<.001					
	DrugB	90	-1.11	2.57	-1.04	0.23	<.001	0.21	0.31	.495	(	-0.40, 0.83)
	Total	180	-1.31	2.59			<.001					
5 (2.0)	DrugA	95	-1.59	2.73	-1.41	0.24	<.001					
	DrugB	95	-1.46	2.84	-1.29	0.23	<.001	0.13	0.33	.700	(	-0.52, 0.78)
	Total	190	-1.53	2.78			<.001					
Overall	DrugA	94	-1.97	2.45	-1.78	0.24	<.001					
	DrugB	91	-1.85	3.04	-1.72	0.24	<.001	0.06	0.34	.853	(	-0.61, 0.73)
Model: Lab Change from Baseline = Baseline + Intervention Group + Visit + Region + Intervention Group*Visit; Covariance Structure = Heterogeneous autoregressive (1st order) type.												

FIGURE: 2 - Last page of the report:

Analysis of Laboratory Analyte Change from Baseline - MMRM

ITT Patients

ABC-DE-FGHI

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Laboratory Analyte: THYROXINE, TOTAL (T4)(nanomole/Liter)

Visit (Week)	Drug Group	N	Mean Change	SD	LS Mean Change	SE	Within Grp p-value [a]	LS Mean Change Difference	SE	Between Grp p-value [b]	95% CI
20(52.0)	DrugA	75	1.11	21.31	3.68	1.92	.057				
	DrugB	72	4.24	16.69	3.00	1.93	.123	-0.68	2.72	.802	(-6.05, 4.69)
	Total	147	2.64	19.19			.097				
Overall	DrugA	75			3.68	1.92	.057				
	DrugB	72			3.00	1.93	.123	-0.68	2.72	.802[c]	(-6.05, 4.69)

Model: Lab Change from Baseline = Baseline + Intervention Group + Visit + Region + Intervention Group*Visit;

Covariance Structure = Unstructured.

Let us see step-by-step processing to generate reports as per above figures.

*** STEP-1: Find out the distinct Lab tests present in the Lab data. For example, let's assume there are 100 distinct Lab tests present;

```
proc sort data=lab out=test nodupkeys;
    by lbtest;
run;
```

*** STEP-2: Find out the number of Lab Tests present in Lab data

*** as there are 100 distinct Lab tests present in the data, macro variable Max will have value 100;

```
proc sql;
    select count(distinct lbtest) into : max from test;
quit;
```

*** STEP-3: create macro variable CD having value of Lab test and TEXT having value of Lab test description to display in the report

*** lab test is sorted in alphabetical order in TEST data, so it will create macro variable for example :cd1 having value as ALBUMIN, cd2 having value as ALT/SGPT,...,cd100 having value as THYROXINE, TOTAL (T4);

```
data _null_;
    set test;
```

*** _N_ is automatic variable and created automatically by the DATA step.

It is initially set to 1. Each time the DATA step loops past the DATA statement, the variable _N_ increments by 1. The value of _N_ represents the number of times the DATA step has iterated.;

```
call symputx ("cd"||compress(put(_n_,8.0)),compress(lbtest),'g');
call symputx ("text"||compress(put(_n_,8.0)),lbunit,'g');
run;
```

*** STEP:4 - create %DO loop which runs from 1 to MAX(max macro variable created in Step-2 above) maximum number of Lab test count;

```
%do i = 1 %to &max; *** %do loop will iterate 100 times as &max has value 100 as per Step-1;
```

```
data labs_final;
```

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*** Where condition will subset data for each lab test after resolving &&cd&i. macro variable. For example, for i = 1, it resolves to cd1 having value as ALBUMIN, cd100 having value as THYROXINE, TOTAL (T4) and so on;

```
set lab(where = (lbtest = "&&cd&i."));
run;
```

```
***...
```

```
...
...;
```

*** add other analysis steps to perform MMRM analysis using PROC MIXED and other data steps as needed above;

*** STEP:5 - create final dataset for each lab test, which will be passed to PROC REPORT;

```
data &&cd&i;
  set final_data;
  ord1 = ceil(_n_/15);
```

*** &covariance has value of Covariance structure for which particular lab test converges using PROC MIXED MMRM analysis like Unstructure, Autoregressive(1), Toeplitz, Compound Symmetry, Heterogeneous Compound Symmetry;

```
c0 = "&covariance.";
```

```
rename week = c1 trt = c2 count1 = c3 mean_change1 = c4 sd_change1 = c5
  chg_estimate = c6 se = c7 ls_pval = c8 diff_estimate = c9 se1 = c10
  diff_pval = c11 conf_int1 = c12;
```

```
run;
```

```
%end;
```

*** STEP:6 - generating report for each lab test using PROC REPORT;

*** STEP:7 - create %DO loop which runs from 1 to MAX(max macro variable created in Step-2 above) maximum number of Lab test count;

```
%do i = 1 %to &max; *** %do loop will iterate 100 times as &max has value 100 as per Step-1;
```

*** STEP:8 - creating macro variable covariance to display in the footnote;

```
data _null_;
  set &&cd&i.;
```

*** c0 variable has value of covariance structure for particular lab test as per STEP-5 above, macro variable covariance will have value of covariance structure;

```
call symputx ("covariance",c0,'g');
run;
```

```
%put &covariance;
```

*** For i = 1, proc report will generate report for Lab test = ALBUMIN,

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for i = 100, proc report will generate report for Lab test = THYROXINE, TOTAL (T4) and so on;

```
proc report data = &&cd&i. headline missing nowindows split = "#";
  column ord1 c1 - c12;

  define ord1/order order = data noprint;
  define c1/"#Visit#(Week)" width = 9 left flow order order=data spacing = 1;
  define c2/"Drug#Group" width = 10 center spacing = 1;
  define c3/"##N" width = 5 center spacing = 1;
  define c4/"#Mean#Change" width = 9 center spacing = 1;
  define c5/"##SD" width = 9 center spacing = 1;
  define c6/"#LS Mean#Change" width = 9 right spacing = 1;
  define c7/"##SE" width = 9 center spacing = 1;
  define c8/"Within Grp# p-value#[a]" width = 10 center spacing = 1;
  define c9/"LS Mean#Change#Difference" width = 10 right spacing = 1;
  define c10/"SE" width = 9 center spacing = 1;
  define c11/"Between Grp# p-value# [b]" width = 11 spacing = 1;
  define c12/"## 95% CI" width = 20 center spacing = 1;

  break after c1/skip;

  compute before _page_;
    line @2 " ";
    line @2 133*" -";

  *** For i = 1, Laboratory Analyte: &&text&i. resolves to Laboratory Analyte:
  ALBUMIN(gram/Liter), for i = 100, it will resolves to Laboratory Analyte: THYROXINE,
  TOTAL (T4)(nanomole/Liter) and so on;

    line @2 "Laboratory Analyte: &&text&i.";
    line @2 133*" -";
  endcomp;

  compute after _page_;
    line @2 133*" -";
    line @2 "Model: Lab Change from Baseline = Baseline + Intervention Group + Visit
+ Region + Intervention Group*Visit;";

    *** &covariance will resolve to appropriate covariance structure as per STEP-8
    above ;
    line @2 "Covariance Structure = &covariance.";
  endcomp;

run;

%END;
```

CONCLUSION (HEADER 1)

This paper mainly concludes:

- It explains how programmers can use %DO loop with Call Symputx to generate MMRM reports for Multiple Lab tests, Vital parameters, and questionnaires.
- In Clinical Research Organizations, there is core demand of standardizing this kind of complex task to save time and increase productivity.

The logic provided with this paper has been tested under a wide variety of situations, and can be used to streamline work whenever such analysis is required.

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REFERENCES

Paper 198-30: Guidelines For Selecting The Covariance Structure In Mixed Model Analysis by Chuck Kincaid, Comsys Information Technology Services, Inc., Portage, MI

PharmaSUG 2015 – SP02 - MMRM: Macro for selecting best covariance structure with the method of interest by Linga Reddy Baddam, Sudarshan Reddy Shabadu, Chunxue Shi
<http://www.pharmasug.org/proceedings/2015/sp/pharmasug-2015-sp02.pdf>

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RECOMMENDED READING

Mixed effect Model Repeat Measurement (MMRM) and Random Coefficient Model Using SAS:
<http://onbiostatistics.blogspot.in/2014/06/mixed-effect-model-repeat-measurement.html>
<https://www.amstat.org/sections/srms/proceedings/y2008/files/301885.pdf>

Paper 113-2011 - %DO Loop – a Simple Dynamic Programming Technique by Yunchao (Susan) Tian, Social & Scientific Systems, Inc., Silver Spring, MD

PharmaSUG2011 - Paper CC18: SYMPLY PUT: GET the most out of SYMPUTX and SYMGETN by Robert Howard, Veridical Solutions, San Diego, CA

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