

Summarizing Data for a Systematic Review

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BACKGROUND

Systematic reviews have become increasingly important in healthcare, particularly when there is a need to compare new treatment options and to justify clinical effectiveness versus cost. This paper describes a method in SAS/STAT® 9.2 for computing weighted averages and weighted standard deviations of clinical variables across treatment options while correctly using these summary measures to draw accurate statistical inference.

The analyses of data from systematic reviews typically involve computations of weighted averages and comparisons across treatment groups. However application of the TTEST procedure does not currently take into account weighted standard deviations when computing P-values. The use of a default non-weighted standard deviation can lead to incorrect statistical inference.

In this paper we have chosen to make statistical comparisons using a student's T-test to generate P-values. When performing a T-test, SAS generally takes the correct weighted averages. However the default standard deviation is an unweighted standard deviation. The use of unweighted standard deviations can lead to erroneous results. The goal of this paper is to introduce an automated method to use the (correct) weighted standard deviation in the computation of the P-values using SAS.

METHOD

Given a dataset containing clinical variables for three treatment options, we wish to make pairwise comparisons of three independent treatments. This is done by creating two temporary datasets using **PROC MEANS** which yields the weighted means and weighted standard deviations.

Subsequently, we then perform a T-test on each temporary dataset. The resultant datasets containing all clinical comparisons of each treatment option are merged and then transposed to obtain the necessary statistics.

The current methods for a meta-analysis require many repetitive steps which are not automated. Performing a meta-analysis requires calculation of weighted averages and weighted standard deviations for each variable of interest followed by performing the statistical testing for the calculation of P-values.

Step 1:

A dataset which contains the desired clinical variables of interest from the clinical literature for 3 different types of surgical approaches (Abdominal, Laparoscopic and Robotic Surgery) was created.

Using this dataset a MEANS Procedure is run with the option VARDEF=WGT. This allows us to compute the weighted means and weighted standard deviations for all the clinical variables of interest stratified by treatment group (Abdominal, Laparoscopic and Robotic Surgery).

Once the weighted means and weighted standard deviations are computed they are stored in a dataset called Mean_clinical with the use of an output statement. This dataset is used in subsequent steps.

Step 2:

The TTEST procedure is run on the previously created dataset from step-1 (Mean_clinical). From the output of this T-test we generate three separate datasets which contain the following:

The first dataset contains the values of the F-statistics, the degrees of freedom and associated P-values for each comparison. The second dataset contains the values of the T-statistics under the conditions of equal variances (Pooled) and unequal variances (Satterthwaite) for each clinical variable. The third dataset contains the weighted means and weighted standard deviations for each variable as well as pairwise difference.

Step 3:

In this step we merged the three outputs from the TTEST procedures described in step 2. We use an IF THEN ELSE conditional statement to choose the appropriate p-value (Pooled or Satterthwaite) based on whether or not the F-statistic is significant. The resulting merged dataset will contain the Pooled and Satterthwaite P-values along with sample size (N), weighted mean and weighted standard deviation.

Step 4:

In this step the RETAIN statement is used to keep the P-values based on the conditional IF THEN ELSE statement used in step-3. All blank P-values (that didn't meet the conditional if then else statement in step-3) are dropped. This results in a dataset that contains the clinical variables of interest and their correct corresponding P-value.

Step 5:

The purpose of this step is to transpose the original dataset Mean_clinical and to merge this file with the dataset Retain_clinical. This will give us all the desired statistics and the correct P-values in one dataset in the desired format for comparisons of two cohorts/groups.

In the case of higher dimensions (comparison of 3 or more groups) an additional step similar to step 5.1 in the source code should be carried out. This involves a double transpose of the two datasets followed by the merging of two transposed datasets.

Step 6:

The REPORT procedure is used to format the final output with the respective P-values and the cohorts/groups. Complete source code is provided in Appendix 1.

RESULTS

The resulting output provides pairwise comparisons of each treatment option and uses the weighted standard deviations to yield the correct P-values in a desired format.

TABLE 1: Comparison of Three Cohorts for Prostatectomy

variable	stats	Laparoscopy	Abdominal	Robotic	p-value
Overall PSM (%)	Number of Cohorts	81	61	73	<0.0001*
	Number of Patients	33,180	47,103	28,950	<0.0001**
	Mean	20.4	24.2	16.2	-
	StdDev	5.0	9.8	5.6	-
Blood Transfusions (%)	Number of Cohorts	79	85	70	0.006*
	Number of Patients	25,610	84,848	5,849	<0.0001**
	Mean	4.7	16.5	1.8	-
	StdDev	6.7	12.5	1.8	-
Complications (%)	Number of Cohorts	57	39	42	0.04*
	Number of Patients	16,389	16,647	14,309	<0.0001**
	Mean	11.1	17.9	7.8	-
	StdDev	9.6	9.1	6.3	-

PSM = Positive Surgical Margins. P-values for: *Laparoscopy vs. Robotic **Abdominal vs. Robotic.
Tewari et al. (2012) Eur Urol. 62(1):1-15.

CONCLUSION

This research provides a simple way of summarizing data from multiple treatment groups from a systematic review while making use of the correct weighted standard deviations using PROC MEANS and PROC TTEST to draw accurate statistical inference.

REFERENCES

[1]. <https://support.sas.com/rnd/app/examples/STATexamples.html>

[2]. A. Tewari, P. Sooriakumaran, D.A. Bloch, U. Seshadri-Kreaden, A.E. Hebert, P. Wiklund. Positive surgical margin and perioperative complication rates of primary surgical treatments for prostate cancer: a systematic review and meta-analysis comparing retropubic, laparoscopic, and robotic prostatectomy. Eur Urol. 2012; 62(1):1-15

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Appendix 1: Source Code

```
/*Step 1: Calculate weighted means and weighted standard deviations using proc means.*/

DATA Data_Clinical;
    SET clinical;
    if Excluded ne . or surgerytype in("Laparoscopy") then delete;
RUN;

PROC SORT;
    by surgerytype;
RUN;

PROC MEANS DATA=Data_Clinical VARDEF=WGT;
    CLASS surgerytype;
    VAR Overall_PSM Blood_Transfusions Complications;
    WEIGHT StudysizeN;
    OUTPUT OUT=Mean_Clinical;
RUN;

/*Step 2: Perform a t-test on each temporary dataset using proc ttest.*/

PROC TTEST DATA=Mean_Clinical;
    ODS OUTPUT ttests=ttests_Clinical
    Statistics=statistics_Clinical equality=equality_Clinical;
    CLASS surgerytype;
    VAR Overall_PSM Blood_Transfusions Complications;
RUN;

/*Step 3: Merge the datasets and use an "if condition" to calculate the p-value.*/

DATA Merge_Clinical;
    MERGE ttests_Clinical statistics_Clinical equality_Clinical;
    BY variable;
    IF probf < .05 THEN method="Satterthwaite";
    ELSE method="Pooled";
    IF method="Pooled" and variances="Equal" THEN PUT probt;
    ELSE IF method="Satterthwaite" and variances="Unequal"
    THEN PUT probt;
    ELSE probt='';
RUN;

/*Step 4: To order the P-values and retain missing values.*/

DATA Retain_Clinical;
    SET merge_Clinical;
    BY variable;
    RETAIN first_non_miss_value;
    IF first.variable THEN first_non_miss_value = .;
    IF first_non_miss_value = . and probt ne . THEN first_non_miss_value = probt;
```

```

        IF last.variable THEN OUTPUT;
RUN;

/*Step 5: Transpose the mean output and merge with the retained output.*/

PROC TRANSPOSE DATA=mean_Clinical OUT=Trans_Clinical;
    BY _stat_;
    VAR Overall_PSM Blood_Transfusions Complications;
    ID Surgerytype;
RUN;

DATA final_Clinical;
    MERGE TRANS_Clinical Retain_Clinical(keep=variable Pvalue);
    BY variable;
RUN;

/*Step 5.1 :To compare more than 3 or more groups */

/*Transpose the final data sets(final_dataset1 comparing Abdominal and Robotic Surgery
and final_data2 Comparing the laparoscopy and Robotic surgery types)created for 2
cohorts */

PROC TRANSPOSE DATA=final_dataset1 OUT=Trans_dataset1;
    BY variable pvalue;
    VAR Abdominal Robotic;
    ID _stat_;
RUN;

PROC TRANSPOSE DATA=final_dataset2 OUT= Trans_dataset2;
    BY variable pvalue;
    VAR Laparoscopy Robotic;
    ID _stat_;
RUN;

PROC SORT DATA= Trans_dataset1;
    BY variable;
RUN;

PROC SORT DATA= Trans_dataset2;
    BY variable;
RUN;

/*Merging the two transposed datasets*/
DATA Merge_dataset12 Rename=(_name_=surgery type));
    LENGTH _NAME_ $20.
    MERGE Trans_dataset1 Trans_dataset2;
    BY _name_;
RUN;

/*Transposing the merged dataset*/

PROC TRANSPOSE DATA= Merge_dataset12 OUT=Output_dataset12 ;
    BY variable;
    VAR N Sumwgt Mean Std;
    ID surgerytype;
RUN;

/*Merging output transposed and the merged dataset of the cohorts*/

DATA final_dataset12 ;
    MERGE Output_dataset12
        Merge_dataset12 (keep=variable pvalue);
    BY variable;

```

```
RUN;

DATA final_dataset12;
    RETAIN variable name Laparoscopy Abdominal Robotic pvalue;
    LENGTH _name_ $20;
    SET final_dataset12;
RUN;

/*Step 6: Format the output report*/
PROC REPORT DATA=final_Clinical NOWD HEADSKIP;
    COLUMN variable stats Laparoscopy Abdominal Robotic pvalue;
    DEFINE variable /ORDER WIDTH=10;
    DEFINE Laparoscopy / FORMAT=6.4;
    DEFINE Abdominal / FORMAT=6.4;
    DEFINE Robotic / FORMAT=6.4;
    DEFINE pvalue /ORDER FORMAT=6.4;
RUN;
```