**Subgroup Analysis Diagnostics Overview**

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| --- | --- |
| **Diagnostic Plot** | **Purpose** |
| TABLE 1 | “Table 1. Baseline Characteristics” before and after propensity score weighting. Population characteristics are typically illustrated in a baseline characteristics table that displays measures of center and spread like means, medians and standard deviations. Propensity score balancing weights, such as overlap weighting, shift the population with respect to baseline characteristics. The weighted baseline table is provided to review the resulting target population.   * Moments that describe the tails of the distribution (5th and 95th percentiles) are included, as modern weighting methods are designed to reduce the influence of outlying values and may therefore changes the boundaries of the population. * Absolute standardized mean differences (ASMD), before and after weighting, are included as a summary of mean balance. * Table 1 is provided for the overall population and BY subgroups so that investigators can understand who is included in the subgroup-specific target population whenever subgroup causal effects are desired. |
| CONNECT-S | Connect-S plot for *S* subgroups resembles the rectangular grid of a Connect4 game: each row represents a subgroup variable (eg, age, sex, race group), and the name is displayed at the beginning of each row; each column represents a confounder that we want to balance (eg, age). Therefore, each dot corresponds to a specific subgroup *S* and confounder *X*, and the shade of the dot is coded based on the absolute standardized mean difference (ASMD) of confounder *X* in subgroup *S*, with darker color meaning more severe imbalance. The end of each row also presents an approximate effective sample size (after weighting the effective sample size may be different from the original sample size) and subgroup-specific approximate variance inflation. The CONNECT-S plot is described in more detail here:  <https://onlinelibrary.wiley.com/doi/full/10.1002/sim.9029> |
| HISTO-LAP | Histograms (HIST) display the overlap (LAP) in continuous covariates between treated and untreated patients, before and after weighting, in a grid for the overall population and subgroups. These plots facilitate visualization of the comparability between treated and untreated patients both in the underlying data and after adjustment. QQ-plots and cumulative density curves have been used for the same purpose, but these tools are less intuitive to a clinical audience. A histogram is among the most clinically intuitive methods for illustrative a distribution.   * Obtain HISTO-LAP on the propensity score (Default) to see how the probability of being treated initially differs and is addressed by weighting. * Obtain HISTO-LAP on any prognostic score (or continuous covariate) to see how the probability of outcome, as predicted by the prognostic score, initially differs and is addressed by weighting. This step is particularly valuable because a prognostic score captures confounding in a way that is strongly related to outcome and the HISTO-LAP will demonstrate comparability (or lack of) across the whole distribution of the prognostic score, rather than just mean balance. * Use the grid to identify subgroups where there is initially too little data or too little overlap to achieve comparability via weighting. These subgroups should not be interpreted. |

**diagSGA macro**

1. **Macro Overview**

The diagSGA macro can be used as a diagnostic tool in propensity score weighting analyses with subgroups. The macro allows to assess the balance of confounders before and after weighting in the overall analysis population and within each subgroup. Using the macro the following output can be produced:

* Tables with descriptive statistics of confounders in unweighted and weighted samples by treatment. Separate tables are generated for each subgroup and the overall sample. Descriptive statistics include mean, median and the 5th and 95th percentiles for continuous variables and percentages for categorical variables. Unweighted and weighted standardized differences are also computed.
* connectS plots for displaying standardized differences by subgroups
* Histograms of propensity scores/prognostic variable comparing treatments in each subgroup.

1. **Input Dataset**

A typical input dataset for the macro should contain one record per observation in the analysis population and the following variables (columns):

One variable identifying treatment or the groups being compared coded as 0/1

One column for each confounder to be included in tables and figures. Confounders can be continuous variables (numeric) or categorical variables (numeric or character).

One column for each variable defining subgroups. A subgroup level represents a subset of the analysis population. For example: men or age > 55. Variables defining subgroups might also be included as categorical confounders.

At least one of the following:

A numeric variable containing weights

A numeric variable containing a propensity score, defined as the probability of treatment = 1.

1. **Macro Parameters**

|  |  |
| --- | --- |
| **Parameter** | **Description** |
| DS | Input dataset as described in #2 above |
| TRTVAR | Numeric variable identifying treatments or groups to be compared. Coded as 0/1. |
| WEIGHTS | Numeric variable containing weights to be applied to observations in the analysis population. |
| PROPENS | Numeric variable containing the propensity score (prob[TRTVAR=1]). If both WEIGHTS and PROPENS are provided, WEIGHTS take priority and the variable provided in PROPENS is not used to compute weights |
| W\_TYPE | Type of weights to be computed in case of WEIGHTS not provided. For overlap weights request W\_TYPE=O, and for IP weights request W\_TYPE=I. Default is W\_TYPE=O. |
| CONTCONF | continuous confounders: list of variable separated by blanks |
| CATCONF | categorical confounders: list of variables separated by blanks |
| SUBGRPS | Variables identifying subgroups: list of variables separated by blanks Subgroups are created for each level of each variable listed in this parameter |
| PROGNOS | Continuous variable considered a prognostic score to be used for histograms plots (optional) |

The following parameters are used to control the destination of output produced and aspect of figures. All parameters are optional.

|  |  |
| --- | --- |
| **Parameter** | **Description** |
| OUTDIR | Location (folder) where the output will be saved. If no folder provided, output will be saved in the same folder as the SAS program. |
| NAME | Descriptive name for the output generated. It will be used to create the names for files. Example: name\_table, name\_connectS\_plot, etc. Default: analysis |
| CONFFMT | Character format assigned to confounders. The format is used to label confounders in cases where variable names are not descriptive enough. For example, if X1 represent age, create a character format assigning “X1” = “Age”. |
| SUBGFMT | Numeric format assigning names to subgroup levels. Subgroups levels are numbered from 1 to K (where K is the total number of subgroups) based on the subgroup variable order provided in the SUBGRPS parameter. For example, if 4 binary variables (B1, B2, B3, B4) are included in SUBGRPS parameter, subgroup levels will be numbered from 1 to 8 with 1 and 2 corresponding to the two levels of B1, etc. An additional level (numbered K+1) is created for the overall analysis population. In this example, the subgroup level would be coded as 9. |
| TRTFMT | Numeric format used to label the treatments being compared |
| COLOR | Flag indicating if the connectS and histogram plots are color or black/white (gray scale). COLOR=Y produces color plots for histograms and color and grey scale plot for connectS plots. COLOR=N produces gray scale plots only. Default is COLOR=N. |
| **connectS plots options** | |
| VI | Flag (Y/N) requesting the variance inflation to be included in connectS plot for the weighted standardized differences. Default is Y. |
| SS | Flag (Y/N) requesting the sample size to be included in connectS plot for the unweighted and weighted standardized differences. For the unweighted connectS plot the actual sample size is displayed. For weighted connectS plot the effective sample size is displayed. Default is Y. |
| HGT | Height in inches for the connectS plot. By default, the height of the connectS plot is set to 0.4\*[number of subgroup levels in the plot (K) + 1] |
| WDT | Width in inches for the connectS plot. By default, the width of the connectS plot is set to 0.4\*[number of confounders in the plot] |
| REFLINES | Allows to specify values where horizontal lines dividing subgroups in the connectS plot will be drawn. For example, REFLINES=2.5 4.5 6.5 will draw horizontal lines between the second and third subgroup, the fourth and fifth subgroup and the sixth and seventh subgroup. Default is no horizontal lines. |
| FSIZE | Controls the size of labels. Default is 8 points for labels and 6 points (75% of 8 points) for variance inflation and sample size. |
| CSIZE | Controls the size of circles in the connectS plot. Default is 12. |
| **Histogram plots options** | |
| NROWS NCOLS | Number of rows and columns for the array of histograms. Either both parameters or none should be provide. If both parameters are not provided then the histograms are arranged in an approximately square figure. |
| XMIN | Minimum value to use for the X-axis in the histogram of the prognostic score |
| XMAX | Maximum value to use for the X-axis in the histogram of the prognostic score |
| XSTEP | Distance between tick marks in the X-axis |
| HXLABEL | Label for the X-axis of the histogram of the prognostic score. Default: variable name |

1. **Macro Output**

Output generated includes:

* A table with unweighted and weighted descriptive statistics (mean, median and 5th and 95th percentiles for continuous confounders and percentages for categorical confounders) along with standardized differences. Separate sections are generated for each subgroup level and one for the overall analysis population. The output is an RTF format document named “*name*\_table.rtf” where *name* is specified with the NAME= parameter.
* A connectS plot for unweighted standardized differences in PNG format named “*name*\_connect\_unweighted.png”.
* A connectS plot for weighted standardized differences in PNG format named “*name*\_connect\_weighted.png”.
* If a propensity score was specified (with the PROPENS= parameter), a histogram comparing the distribution of the weighted propensity score between the two treatments in each subgroup and the overall analysis population. The PNG format output will be named “*name*\_propensity\_histograms.png” where *name* is specified with the NAME= parameter.
* If a prognostic score was specified (with the PROGNOS= parameter), a histogram comparing the distribution of the weighted prognostic score between the two treatments in each subgroup and the overall analysis population. The PNG format output will be named “*name*\_*prognos*\_histograms.png” where *name* is specified with the NAME= parameter and *prognos* is the variable name for the prognostic score.

1. **Illustration with simulated data**

The simulated dataset (*SGAexample*) contains 3000 rows with each row representing one observation or individual. There are 21 variables (columns), including 20 covariates and 1 binary treatment. The binary variable is named *Treatment* and coded 1 for a new treatment and 0 for placebo.  
Variables X1-X18 are confounders among which X1-X8 are binary and X9-X18 are continuous. The prespecified subgroups are defined by binary variables X1-X3 and X19-X20. The table shows the first 5 records for the simulated dataset.

| Treatment | X1 | X2 | X3 | X4 | X5 | X6 | X7 | X8 | X9 | X10 | X11 | X12 | X13 | X14 | X15 | X16 | X17 | X18 | X19 | X20 |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 53 | 52 | 11 | 99 | 72 | 38 | 95 | 85 | 73 | 26 | 0 | 0 |
| 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 63 | 46 | 14 | 88 | 67 | 34 | 117 | 88 | 69 | 26 | 1 | 1 |
| 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 68 | 42 | 13 | 106 | 60 | 33 | 112 | 73 | 58 | 23 | 0 | 0 |
| 1 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 48 | 49 | 14 | 97 | 65 | 35 | 109 | 84 | 59 | 24 | 1 | 0 |
| 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 64 | 52 | 11 | 91 | 70 | 36 | 116 | 72 | 76 | 27 | 1 | 0 |

The propensity scores can be estimated using a main effects logistic regression model:

proc logistic data=SGAexample;

model Treatment(event="1") = X1-X18;

output out=propensity p=ps;

run;

**5.A. Bare Bones Example**

A simple call to the diagSGA macro would be:

%diagSGA(ds=propensity, propens=ps, trtvar=Treatment,

contconf=x9 x10 x11 x12 x13 x14 x15 x16 x17 x18,

catconf=x1 x2 x3 x4 x5 x6 x7 x8 x19 x20,

subgrps=x1 x2 x3 x19 x20);

Figure 1 shows a sample of one of the tables generated. Figures 2 and 3 show the unweighted and weighted connectS plots and Figure 4 shows the histograms comparing weighted propensity scores by subgroup and treatment.

Table

Description automatically generatedTable 1. Descriptive statistics and standardized differences for bare bones example (table section)

Background pattern

Description automatically generatedFigure 2. CONNECT-S plot with unweighted standardized differences for bare bones example

Background pattern

Description automatically generatedFigure 3. CONNECT-S plot with weighted standardized differences for bare bones example

Figure 4. HISTO-LAP histogram with weighted propensity score by subgroup and treatment for bare bones example

**Diagram

Description automatically generated**

**5.B. Enhanced Example**

Adding a few parameters to the macro call can substantially enhance the look of the output. It is recommended that formats are provided for the confounders names, subgroup names and treatment names. For example, assuming that variables X1 to X8 represents patients characteristcs or comorbidities, X9 to X18 vitals and labs and X19 and X20 concomitant medications. The following formats can be used.

proc format;

value $conf "x1"="Sex" "x2"="Race" "x3"="Diabetes" "x4"="Hypertension"

"x5"="PAD" "x6"="Prior MI" "x7"="Prior Stroke" "x8"="COPD"

"x9"="Age" "x10"="HDL-C" "x11"="Hemoglobin" "x12"="Glucose"

"x13"="eGFR" "x14"="Sodium" "x15"="SBP" "x16"="DBP"

"x17"="Heart Rate" "x18"="BMI" "x19"="Beta Blockers"

"x20"="Statins";

value sub 1="Sex: Male" 2="Sex: Female" 3="Race: White" 4="Race: Non-White"

5="Diabetes: No" 6="Diabetes: Yes" 7="Beta-Blockers: No"  
 8="Beta-Blockers: Yes" 9="Statins: No" 10="Statins: Yes" 11="Overall";

value tx 1="New Treatment" 0="Placebo";

run;

The following macro call generates the output displayed in Figures 5-8.

%diagSGA(ds=propensity,propens=ps,w\_type=O,trtvar=Treatment,

contconf=x9 x10 x11 x12 x13 x14 x15 x16 x17 x18,

catconf=x1 x2 x3 x4 x5 x6 x7 x8,

subgrps=x1 x2 x3 x19 x20,

conffmt=$conf,subgfmt=sub,trtfmt=tx);

Table

Description automatically generatedFigure 5. Descriptive statistics and standardized differences for enhanced example (table section)

Background pattern

Description automatically generatedFigure 6. CONNECT-S plot with unweighted standardized differences for enhanced example

Background pattern

Description automatically generated with medium confidenceFigure 7. CONNECT-S plot with weighted standardized differences for enhanced example

Diagram

Description automatically generatedFigure 8. HISTO-LAP histogram with weighted propensity score by subgroup and treatment for enhanced example

**5.C. Bells and Whistles Example**

This example shows some additional macro parameters that can be used to customize the output.

%diagSGA(ds=propensity,propens=ps,w\_type=O,trtvar=Treatment,

contconf=x9 x10 x11 x12 x13 x14 x15 x16 x17 x18,

catconf=x1 x2 x3 x4 x5 x6 x7 x8,

subgrps=x1 x2 x3 x19 x20,

prognos=x12,

outdir=/../output/example/,name=bells,

conffmt=$conf,subgfmt=sub,trtfmt=tx,

reflines=%str(2.5 4.5 6.5 8.5 10.5),

fsize=7,csize=15,

xmin=50,xmax=130,xstep=20,hxlabel=%str(Glucose),

color=Y);

Figures 9 and 10 present selected output from the previous macro call.

A picture containing diagram

Description automatically generatedFigure 9. CONNECT-S plot with weighted standardized differences for bells and whistles example

Timeline

Description automatically generatedFigure 10. Histogram with weighted prognostic score (Glucose) by subgroup and treatment for bells and whistles example

1. **Comments**

Categorical confounders with more than 2 levels can be included in two different ways: as a character variable formatted with the levels labeled (for example, race\_c with levels “White” “African American” and “Other”) or as dummy variables representing each level of the confounder. Subgroups variables with more than 2 levels should be included as one numeric variable.

The computation of standardized differences is based on a modified version of SAS macro stddiff.sas available at <https://www.lerner.ccf.org/qhs/software/>.

It is recommended to delete any record with missings in one or more of the variables used in the macro call.