

Exploratory Meta Analysis on Uniform Assessment Battery across Aging Studies

Meta-analyses may be conducted to study the consistency of the exact same outcome measure or relationship between measures across studies from different subject populations. For example, a total number of n studies (Study1, Study2, Study3 ... and Studyn) are conducted in elderly population with different comorbidities (e.g. COPD, Heart Failure, at risk of CVD, self-reported moderate disability). Associations of a certain set of continuous outcomes (Y_1, Y_2, \dots, Y_{ny}) with a certain set of predictors (X_1, X_2, \dots, X_{nx}) are investigated within each study. If the measurements of Y_i 's and X_j 's are exactly the same for these studies then they form a **uniform assessment battery**. Y_i 's form the **response battery** and X_j 's form the **predictor battery**. It might be of interest to explore pair-wise relationships between Y_i 's and X_j 's within each study and whether these relationships are consistent across elderly populations with different comorbidities after adjusting for covariates ($CovX_1, CovX_2, \dots, CovX_{nc}$).

Practically, one needs to fit $ny \times nx$ pair-wise regression models within each study plus a combined regression model for each pair of Y_i and X_j . To avoid the hassle to summarize all these results, this SAS macro (%report0) was written to provide batch processing of regression analyses within each study and for the combined sample for each pair of response and predictor. The output is a nicely layout report table and is ready for publication with minor changes according to investigators' taste.

Example

Evidence shows that inflammation might serve as a common mechanism for functional decline, independent of whether it is initiated by an acute event, chronic disease, or aging. Investigator A has data of uniform assessment battery of inflammatory biomarkers (CRP, IL-6 and TNF- α), physical performance (grip strength, 4 meter walk time, SPPB, and repeated chair rise time), and body composition (measured by DEXA) on four populations of older adults with various aging-related diseases/conditions (Study1, Study2, Study3 and Study4). It is of great interest whether circulating levels of CRP, IL-6 and TNF- α are associated with physical function in older persons, independent of disease status. Given the importance of body fat and lean mass, we also determined whether these associations were independent of body composition. Other covariates available include gender and race.

Data Structure

The data layout should look like the following:

PID	CRP	IL6	TNF_ alpha	Grip	SPPB	fourm_ walk	chairrise	gender	race	studyid	study1	study2	study4
1	0.64958	0.04130	-2.10067	27.4523	8.8550	3.00943	14.0891	0	0	study1	1	0	0
2	-0.52903	-0.47353	-2.15353	32.6434	10.9266	3.32705	11.6317	1	1	study1	1	0	0
3	0.34088	0.20790	-1.08584	21.6040	8.5114	4.13803	13.8948	0	1	study1	1	0	0
4	2.45637	1.58489	-0.92106	15.8761	11.1102	3.18484	11.7026	1	1	study2	0	1	0
5	0.47063	-0.84157	0.06658	30.0759	9.4844	3.56433	17.6159	0	1	study3	0	0	0
6	-0.24653	-0.56551	-0.41186	22.4737	10.8518	4.11864	11.0067	0	0	study4	0	0	1
7	0.13182	0.06458	-0.18072	40.2258	11.5347	3.04040	13.0071	0	1	study1	1	0	0
8	0.60629	-0.30794	0.29721	33.3471	10.8924	3.85593	9.0694	0	0	study2	0	1	0
9	0.75572	-0.20319	0.11677	32.7299	9.0079	3.03675	12.6765	0	1	study4	0	0	4
10	0.86810	-0.63047	-0.34619	25.6197	9.5906	4.06886	12.2226	0	1	study3	0	0	0

Reserved Variable Names

Please note that the following variable names are reserved for this macro:

Nx, Ny, X1, X2, X3,... Xn (n is the number of predictors), Y1, Y2, Y3, ... Ym (m is the number of outcomes), YL1, YL2, YL3,... YLm, and tt.
Except for tt, you need to specify these variables before you run the MACRO. See **Extra SAS codes** below.

Extra SAS codes

Before run the MACRO, you will need to specify some necessary MACRO variables such as:

- * Put the data in your current working space or preferred library;
- * and recode study to make dummy variables;

```
data study;
set study;
study1 = 0; study2 = 0; study4 =0;
if studyid = 'study1' then study1 = 1;
if studyid = 'study2' then study2 = 1;
if studyid = 'study4' then study4 = 1;
run;

* ===== Define MACRO variables =====;
* Number of predictors;
%LET Nx = 3;
* Number of outcomes;
%LET Ny = 4;
* input SAS data for the MACRO;
%LET data = study;
* Specify study indicator;
%LET Studyid = studyid;

%LET Studies = study1 study2 study4;
* Specify predictors Xi's (here biomarkers);
%LET X3 = CRP; %LET X2 = IL6; %LET X1 = TNF_alpha;
* Specify outcomes Yi's (here physical performance);
%LET Y4 = Grip; %LET Y2 = SPPB; %LET Y3 = fourm_walk; %LET Y1 = chairrise;
* Specify labels for outcomes;
%LET YL4 = GRIP; %LET YL2 = SPPB; %LET YL3 = Gait Speed; %LET YL1 = Five Chair Rise Time
(Sec);
* Specify where you want your output file to be saved;
%LET path = C;;
```

Then you can proceed to run the SAS MACRO:

```
* ===== Run the MACRO =====;
%report0(gender race, &data, &Studyid, &Studies, &path);
```

Output bubble plot data:

```
* The macro already generates the output data for bubble plot in MATLAB;
proc export data= tt
  outfile='C:\-path\tt.xls'
  dbms=excel
  replace;
run;
```

Note

You might get warnings or error in SAS log if if certain items were not measured in some of the datasets (such as grip strength for study 2 in the example), but that it won't cause any problems with the macro executing.

SAS output

If you run the MACRO properly the output should be an rtf file and looks like the following:

***Regression Coefficient (SD unit) Adjusted by gender race
as reported on 12/05/08***

		Five Chair Rise Time (Sec)		SPPB		Gait Speed		GRIP	
Items	Study	N	b(p-value)	N	b(p-value)	N	b(p-value)	N	b(p-value)
CRP	Combi	573	0.67 (<.001)	573	-0.24 (<.001)	573	0.18 (<.001)	532	-2.13 (<.001)
	study1	69	0.20 (0.650)	69	-0.07 (0.659)	69	0.02 (0.786)	69	-2.27 (0.025)
	study2	41	1.02 (0.499)	41	0.41 (0.203)	41	-0.28 (0.280)		
	study3	173	0.54 (0.199)	173	-0.19 (0.127)	173	0.19 (0.043)	173	1.17 (0.299)
	study4	290	0.85 (<.001)	290	-0.35 (<.001)	290	0.24 (<.001)	290	-3.93 (<.001)
IL6	Combi	573	1.27 (<.001)	573	-0.29 (<.001)	573	0.11 (0.011)	532	-0.42 (0.490)
	study1	69	0.32 (0.495)	69	-0.24 (0.153)	69	-0.04 (0.636)	69	-0.99 (0.370)
	study2	41	2.77 (<.001)	41	-0.23 (0.166)	41	0.31 (0.016)		
	study3	173	0.92 (0.012)	173	-0.16 (0.139)	173	0.08 (0.344)	173	1.45 (0.141)
	study4	290	1.41 (<.001)	290	-0.49 (<.001)	290	0.13 (0.076)	290	-2.54 (0.008)
TNF_alpha	Combi	283	0.67 (0.042)	283	-0.08 (0.428)	283	0.03 (0.668)	242	-0.59 (0.604)
	study1	69	0.44 (0.393)	69	-0.31 (0.091)	69	0.02 (0.865)	69	1.39 (0.241)
	study2	41	1.84 (0.002)	41	-0.19 (0.141)	41	0.31 (0.002)		
	study3	173	-0.97 (0.113)	173	0.25 (0.176)	173	-0.38 (0.006)	173	-1.94 (0.233)

*: sample size for each study

** : regression coefficient for each study

: study is also adjusted for combined studies.

Bubble Plots

An example of bubble plot for log(CRP) is demonstrated here (Figure 1). The MATLAB program will automatically produce bubble plots for all outcomes.

Sample MATLAB Codes:

```
data = 'C:\tt.xls';  
BubblePlot(data);
```

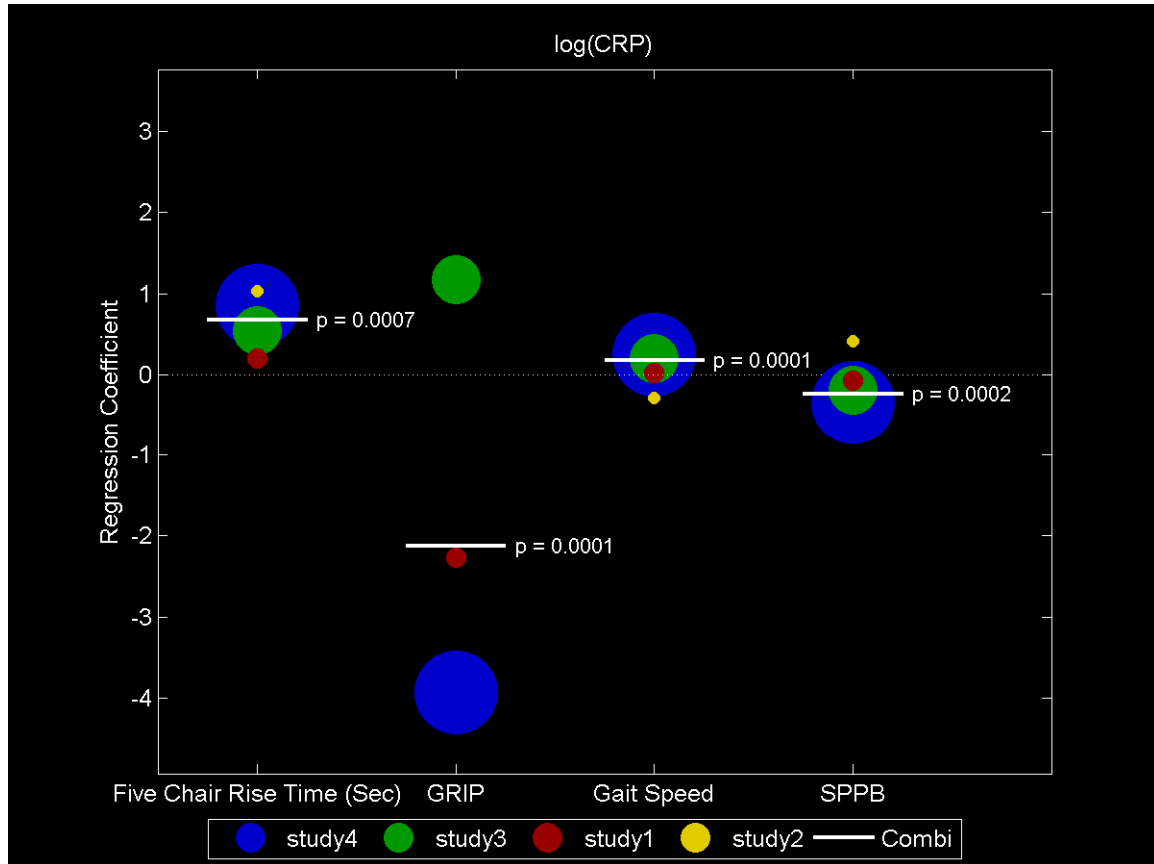


Figure 1. Changes in physical function measures per 1 SD unit difference in log(CRP) after adjustment for gender, and race. In the combined analyses, coefficients are also adjusted for study. P-values are from the test for slope=0 in the combined analyses. The size of the symbol is proportional to the sample size. A positive coefficient for chair rise and walk times and a negative coefficient for SPPB scores and grip strength are indicative of poorer physical function.

Reference

Article Link: http://www.fasebj.org/cgi/content/meeting_abstract/21/6/A1068-a