The SAS METAANAL Macro

Ellen Hertzmark and Donna Spiegelman

March 31, 2017

Abstract

The %METAANAL macro is a SAS version 9 macro that produces the DerSimonian-Laird estimators for random effects or fixed effects models in pooled or metaanalysis. It can be used to pull results from two or three of the Channing cohorts and test for between-studies heterogeneity. Keywords: SAS, macro, metaanalysis, DerSimonian-Laird, inhomogeneity, pooling, fixed effects model, random effects model

Contents

1	Des	cription	2		
2	Invocation and Details				
3 Examples					
	3.1	Example 1. Obesity and lung cancer	5		
	3.2	Example 2. Errors in the macro call	6		
		3.2.1 Example 2a. Did not specify SE_OR_VAR \ldots	6		
		3.2.2 Example 2b. Omitted one of the required parameters	7		
	3.3	Example 3. Using the confidence limits instead of the coefficient and standard error	7		
4	Frequently Asked Questions				
	4.1	Q: The macro formats low p-values as '< .0001', but I need to see the real value $~$	8		
	4.2	Q: What should I do about a variable that is represented as a set of indicators?	9		
5	5 References		9		
6	\mathbf{Cre}	dits	9		

1 Description

This macro produces the Laird and DerSimonian estimators for fixed and random effects models in meta- or pooled analysis. It can be used to pull results from two or three of the Channing cohorts and test for between-studies heterogeneity. Depending on the type of pooling, the studies are weighted proportionately to the inverse of the sum of the study specific variance plus the common between-studies variance (random effects pooling) or the inverse of the study-specific variance (fixed effects pooling).

In using studies from the literature, the macro can take data in the form of 95% confidence intervals or coefficients with standard errors or variances (but not both). The macro can also handle continuous outcomes.

The macro does its calculations for one coefficient at a time.

2 Invocation and Details

To call %METAANAL, your program must know where to look for it. In the Channing Lab, the most efficient way is to include

options mautosource sasautos='/usr/local/channing/sasautos';

at the top of your program.

Below, values to the right of the '=' are the default values for the parameters, if any.

You type

```
%metaanal(
REQUIRED PARAMETERS
_____
 DATA =, name of the dataset containing the coefficients
          and their variances (or however you are providing the data)
          It is desirable that the coefficients and
          their variances have at least 5 significant digits.
          If you are using values from the literature,
          do the best you can.
          REQUIRED
 STUDYLAB = ,
               name of the variable for the labels of the studies.
               REQUIRED
               descriptive title of exposure
 EXPLABEL = ,
               REQUIRED
 OUTCOMELABEL = , descriptive title of outcome
                   REQUIRED
```

OPTIONAL PARAMETERS

COEFF=T, T=results are given as coefficients and standard errors or variances; F=results are given as 95% confidence intervals. OPTIONAL

REQUIRED IF COEFF=T

- BETA = beta, if COEFF=T, the name of the variable for the coefficients This parameter must contain a variable name.
- SE_OR_VAR =V, if COEFF=T, whether you are giving the macro the standard errors (S) or the variances (V) of the coefficients
- VAR = var, if COEFF=T, the name of the variable for the variances of the coefficients This parameter must contain a variable name. REQUIRED if COEFF is T and SE_OR_VAR is V.
- SE = se, if COEFF=T, the name of the variable for the standard errors
 of the coefficients
 This parameter must contain a variable name.
 REQUIRED if COEFF is T and SE_OR_VAR is S.

REQUIRED IF COEFF=F

- VARNAMELCB = if COEFF=F, the name of the variable for the lower 95% confidence bound REQUIRED if COEFF is F
- VARNAMEUCB = if COEFF=F, the name of the variable for the upper 95% confidence bound REQUIRED if COEFF is F

OPTIONAL PARAMETERS

- POOLTYPE = random, method for pooling (random, fixed, or both) The default has been set to random, as that is what we recommend. OPTIONAL
- WT = 1, The difference/change in the exposure for which to compute the odds ratios. If no value is given, the macro will set WT = 1. OPTIONAL
- OUTDAT =, name of a data set to which the results of %METAANAL will be output, if any. If no name is given, no data set will be made. OPTIONAL

```
NOPRINT = F, F=print the output, T=do not print the output
                You might want to use NOPRINT=F if you are making
                an output data set (i.e. outdat has a value).
                If OUTDAT does not have a value, the macro will
                set NOPRINT=F and print a WARNING.
                default=F
                OPTIONAL
 LOGLINEAR = T, T=results are from loglinear models
                  (logistic, phreg, log-binomial, poisson),
                  F=results are from linear models
                  If LOGLINEAR is T, the macro will display the pooled odds ratio or risk ratio
                  and its 95% confidence interval.
                  OPTIONAL
 PRINTCOEFF = F, if LOGLINEAR is T, F=don't print the coefficients, only the RR/ORs.
                                      T=print the coefficients IN ADDITION TO the RR/ORs.
                   OPTIONAL
 PVALUEFORMAT = pvalue6.4 Any legitimate SAS format can be used.
                            Pvalue6.4 is sufficient for most purposes, but
                            can be overridden if you need more precision, e.g.
                            from GWAS.
                            OPTIONAL
);
```

3 Examples

Below we give examples of %METAANAL using data from an analysis pooling NHS and HPFS data from 1986 to 2000. The outcome of interest is confirmed lung cancer among subjects with known smoking status. There were 883 incident lung cancer cases among 330129 person-periods in NHS and 272 among 125371 person-periods in HPFS. For simplicity, the model contains only 3 variables: current smoking (currsmoke) early age (under 15) at start of smoking (agestr1), and obesity (bmige30). As usual, the Cox proportional hazards model is stratified by age in months and time period.

We consider the effect of obesity (bmi ge 30). The analysis was done with the following code:

```
proc phreg data=alldat outest=men;
model ptime*lung19(0)=currsmoke agestr1 bmige30;
where gender eq 1 and bmim ne 1;
run;
proc phreg data=alldat outest=women;
```

```
model ptime*lung19(0)=currsmoke agestr1 bmige30;
where gender eq 2 and bmim ne 1;
run;
```

The dataset, OBESE, used in the calls to %METAANAL is

Obs	beta	se	р	study
1	-0.36254	0.11010	.001	nhs
2	-0.03305	0.22174	.88	hpfs

It was made by appending MEN to WOMEN.

3.1 Example 1. Obesity and lung cancer

The macro call was

```
title2 'example 1';
%metaanal(data=obese, beta=estimate, se_or_var=s, se=stderr, studylab=study,
loglinear=t, coeff=t,
printcoeff=t,
explabel=obesity (BMI ge 30), outcomelabel=lung cancer);
```

Note that we gave the macro the standard errors of the coefficients, rather than the variances, because this was is what we got in the output data set from PROC PHREG. The output was

```
The SAS System
example 1
Studies of obesity (BMI ge 30) and lung cancer
listing of input data
                                              weight in
                                                           weight in
                               std error
                                                fixed
                                                             random
                                of study
                                               effects
                                                            effects
                 Parameter
                              coefficient
                                                             model
Obs
       study
                  Estimate
                                               model
       NHS
                  -0.36254
                                0.11010
                                               0.80222
                                                            0.67063
1
2
       HPFS
                  -0.03305
                                0.22174
                                               0.19778
                                                            0.32937
The SAS System
example 1
Studies of obesity (BMI ge 30) and lung cancer
Obs
       Statistic
                     Value (95% CI)
                                                   Ρ
                                                                     Hypothesis being tested
3
       OR/RR (R)
                     0.78 (0.57, 1.05)
                                                        Is OR/RR different from 1? (Random effects mo
                                              0.1009
                     -0.25 (-0.56, 0.05)
                                                        Is coeff. different from 0? (Random effects mo
4
       Coeff. (R)
                                              0.1009
                                                        Is there heterogeneity among the studies?
5
                     1.77
                                              0.1832
       Q
```

6	tau2	0.0236				
7	r(i)	54.9 (0.0, 100.0)				
8	CVB	0.605 (0.000, 2.663)				
9	r(b)	49.3 (0.0, 100.0)				
The S	AS System le 1					
Studi	es of obesity	(BMI ge 30) and lung can	cer			
Obs	Statistic	Description				
3	OR/RR (R)	OR/RR from random effects model (95% CI)				
4	Coeff. (R)	Coefficient from random effects model				
5	Q	Q-statistic for heterogeneity with 1 degree(s) of freedom				
6	tau2	Estimate of between-studies variance (tau squared)				
7	r(i)	Between-studies variance as a percent of total variance (r(i))				
8	CVB	SQRT(Between-studies variance)/coeff. from random-effects model (CVB)				
9	r(b)	New between-studies variance as a percent of total variance (r(b))				

The title given by the macro used the parameters EXPLABEL and OUTCOMELABEL, so you will know what the analysis was about when you look at it 6 months from now. Then the macro listed the input data. This listing also shows the weights for the fixed effects and random effects models. The big white space before the title is there to allow room for up to 3 user titles. Then the macro gave the results of the random effects model (the default).

3.2 Example 2. Errors in the macro call

3.2.1 Example 2a. Did not specify SE_OR_VAR

In this example, we did not set se_or_var to S, so the macro used the default (v). However, there is no variable VAR (the default name for the coefficient's variance) in the input dataset OBESE.

```
title2 'example 2';
%metaanal(data=obese, beta=estimate, se=stderr, studylab=study,
loglinear=t, coeff=t,
explabel=obesity (BMI ge 30), outcomelabel=lung cancer);
```

In the .log file, we got the following

The SAS System example 2

There is not enough information to do the metaanalysis All values of the variable VAR are missing. All values of the variable STDERR are missing.

Note that the macro thought that all values of STDERR were missing, even though the input dataset has non-missing values. This is because the macro tried to compute STDERR from the missing default variable VAR, and so replaced the original values with missings.

3.2.2 Example 2b. Omitted one of the required parameters

The macro call was

```
title2 'example 3';
%metaanal(data=obese, beta=estimate, studylab=study,
loglinear=t, coeff=t,
printcoeff=t,
explabel=obesity (BMI ge 30));
```

The call did not specify OUTCOMELABEL. This resulted in an error message in the .LOG and the .LST.

3.3 Example 3. Using the confidence limits instead of the coefficient and standard error

For purposes of this example, we calculated the confidence limits from the coefficients and the standard error, then gave these to the macro instead of the coeff, using COEFF=F and giving the values for the upper and lower confidence limits. The macro call is

Obs	study	study coefficient	std error of study coefficient	weight i fixed effects model	in S	weight in random effects model		
1 2	NHS HPFS	-0.36254 -0.03305	0.11010 0.22174	0.80222 0.19778	2 3	0.67063 0.32937		
The S. examp examp Studi	AS System le with co le 4 es of obes	onfidence inter sity (BMI ge 30	vals) and lung can	cer				
Obs	Statist	ic Value (9	5% CI)	Р		Нур	othesis being tested	
1 2 3 4 5 6 7 8 9	OR/RR (I Coeff. (I OR/RR (I Coeff. (I Q tau2 r(i) CVB r(b)	F) 0.74 (0. (F) -0.30 (- R) 0.78 (0. (R) -0.25 (- 1.77 0.0236 54.9 (0. 0.605 (0 49.3 (0.	61, 0.90) 0.49, -0.10) 57, 1.05) 0.56, 0.05) 0, 100.0) .000, 2.663) 0, 100.0)	0.0026 0.0026 0.1009 0.1009 0.1832	Is Is Is Is	OR/RR differ coeff. differ OR/RR differ coeff. differ there heterog	rent from 1? (Fixed effects m rent from 0? (Fixed effects m rent from 1? (Random effects rent from 0? (Random effects reneity among the studies?	100 100 mc mc
The S examp examp Studi	AS System le with co le 4 es of obes	onfidence inter sity (BMI ge 30	vals) and lung can	cer				1
Obs	Statist	ic Descript	ion					
1 2 3 4 5 6 7 8 9	1OR/RR (F)OR/RR from fixed effects model (95% CI)2Coeff. (F)Coefficient from fixed effects model3OR/RR (R)OR/RR from random effects model (95% CI)4Coeff. (R)Coefficient from random effects model5QQ-statistic for heterogeneity with 1 degree(s) of freedom6tau2Estimate of between-studies variance (tau squared)7r(i)Between-studies variance as a percent of total variance (r(i))8CVBSQRT(Between-studies variance)/coeff. from random-effects model (CVB)9r(b)New between-studies variance as a percent of total variance (r(b))							

4 Frequently Asked Questions

4.1 Q: The macro formats low p-values as '< .0001', but I need to see the real value

A: Use the *OUTDAT* parameter to make an output dataset of the results, then reformat the p-value. I suggest making a permanent dataset, so you can play around. Alternatively, you can set pvalueformat=best12. .

4.2 Q: What should I do about a variable that is represented as a set of indicators?

A: You need to make small datasets for each of the indicators. For example, if you have quintile indicators, you have 4 coefficients for each study. You need to make 4 datasets, each of which has the coefficients for one of the quintile indicators.

5 References

DerSimonian, R. and Laird, N.: Meta-analysis in clinical trials. Controlled Clinical Trials 7:177-188, 1986.

Smith-Warner, S.A., Spiegleman, D., Ritz, J., *et al.*: Methods for pooling results of epidemiologic studies: the pooling project of prospective studies of diet and cancer. Am J Epidemiol 163:1053-1064, 2006.

Takkouche, B., Cadarso-Suarez, C., Spiegelman, D.: Evaluation of old and new tests of heterogeneity in epidemiologic meta-analysis. Am J Epidemiol 150(2): 206-215, 1999.

Takkouche, B., Khudyakov, P., Costa-Bouzas, J., Spiegelman, D.: Confidence intervals for heterogeneity measures in meta-analysis. American journal of epidemiology. 2013 Aug 6.

Crippa, A., Khudyakov, P., Wang, M., Orsini, N., Spiegelman, D.: A new measure of betweenstudies heterogeneity in meta-analysis. Statistics in medicine. 2016 Sep 20;35(21):3661-75.

6 Credits

Written by Ellen Hertzmark and Donna Spiegelman for the Channing Laboratory. Questions can be directed to Polyna Khudyakov, stpok@channing.harvard.edu, (617) 432-1822.