

Biography

- ▶ Jagadish Katam is a Principal Statistical Programmer at Princeps Technologies Inc. With more than 8 years experience as SAS programmer and leading studies. He has worked on successful clinical submissions. His expertise ranges from SDTM, ADaM, TFLs and macro programming. He likes to spend his free time in SAS community forum discussions. Nowadays he is also exploring the usage of R in supporting innovative statistical methodologies and advanced visualization in the pharma industry. He sees PHUSE as a good platform to share & gain knowledge on various innovative topics in the ever evolving clinical industry.

Dynamic Macro Using the Convergence Dataset to Generate the Odds Ratio (OR), Risk Ratio (RR) and Risk Difference (RD) per SOC and PT Using the Genmod Procedure

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Agenda

- ▶ Mock Shell
- ▶ Challenges
- ▶ Genmod Procedure
- ▶ Pseudo Code for OR, RR and RD
- ▶ %convergence macro
- ▶ Convergence Dataset
- ▶ %or_rr_rd macro
- ▶ Final Output

Mock Shell

TABLE X

Analysis of Proportion of Subjects with Severe Adverse Events (Maximum Grade 3 or 4)

- by SOC and Preferred Term

System Organ Class Preferred Term	TRT 1 (N=xxx)	TRT 2 (N=xxx)	OR (95%CI)	RD (95%CI)	RR (95%CI)
Gastrointestinal disorders					
Any event	xxx (xx%)	xxx (xx%)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Colitis	xxx (xx%)	xxx (xx%)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Large intestine perforation	xxx (xx%)	xxx (xx%)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Rectal fissure	xxx (xx%)	xxx (xx%)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)

Note: OR = Odds Ratio; RD = Risk Difference (percentages); RR = Relative Risk. RD, OR and RR are obtained from genmod models (link = identity, logit or log, respectively) with no covariate adjustment. NC = Not Calculable. Zero counts for AEs in either treatment group may lead to unreliable statistical estimates.

Challenges

- ▶ Aim is to generate the Odds Ratio (OR), Risk Ratio (RR) and Risk Difference (RD) per SOC and PT using genmod procedure.
- ▶ However when we use the genmod procedure, depending upon the data OR, RR and RD may or may not be obtained.
- ▶ If the given data supports the model in genmod procedure then the OR, RR and RD will be generated, however if given data does not support the model in genmod procedure then no OR, RR and RD will be generated.
- ▶ And, sometimes the given data either supports one or two of (OR, RR and RD).
- ▶ In all the cases, we still need to check the OR, RR and RD for all the SOC and PT and present the output.

Challenges

- ▶ The main challenge is to run the genmod procedure for OR, RR and RD for each SOC and PT.
- ▶ However when we do so depending on the data, if for any SOC or PT either one of or all of genmod procedures for OR, RR and RD may support or may not support the model , if the data does not support the model then it gives error and the program aborts.
- ▶ Also, as per the standards the program executed should not have any errors or warnings in the log.
- ▶ So the program has to be written dynamically in such a way that the genmod procedure need to be executed only for those SOC or PT whose data supports the model and generates the OR, RR and RD.
- ▶ For those SOC or PT data which does not support the model, a dummy data with SOC , PT should be generated for display purpose in the output.

Challenges

- ▶ The plan is to generate the convergence dataset where we can check if the convergence criteria is met in the model or not, since only when the convergence criteria is met, the genmod procedure for OR, RR and RD executes without error or warning.
- ▶ How to check the convergence criteria is met or not?
- ▶ We will see in the genmod pseudo code how we can check the convergence criteria.

Genmod procedure pseudo code for RD

```
proc genmod data = fin;  
class trt01an;  
  model respond = trt01an / dist=bin link=identity type3;  
  estimate "Risk Diff" trt01an 1 -1/exp;  
  ods output Estimates = cpdiff  
               convergencestatus=rd_convergence;  
run;
```

Genmod procedure pseudo code for OR

```
proc genmod data = fin;  
class trt01an;  
  model respond = trt01an / dist=bin type3 ;  
  estimate "Odds Ratio" trt01an 1 -1/exp;  
  Ods output Estimates = ests  
  convergencestatus=or_convergence;  
run;
```

Genmod procedure pseudo code for RR

```
proc genmod data = fin;  
class trt01an;  
  model respond = trt01an / dist=bin link=log type3 ;  
  estimate "Risk Ratio" trt01an 1 -1/exp;  
  ods output Estimates = rrests  
               convergencestatus=rr_convergence;  
run;
```

Respond Variable

- In all the pseudo codes the common variable is the respond variable, which is derived as below

```
data fin;  
merge adsl(in=a) adae(in=b );  
by usubjid;  
if a;  
if a and b then respond=1;  
if a and not b then respond=2;  
run;
```

```
proc sort data= fin ;  
by trt01an respond;  
run;
```

%convergence macro

- ▶ %convergence macro to create the convergence data set for every SOC and PT within the given data.
- ▶ It produces a convergence data set which has SOC and PT variables along with the convergence STATUS variable and STAT variable which has OR, RR and RD values.
- ▶ Example, a typical macro call to create the convergence data set will look like this

```
%convergence (whr=anl07fl="Y",  
              row=row,  
              soc=aesoc,  
              pt=aedecod,  
              subset=) ;
```

%convergence macro

- ▶ The macro expects that the input ADAE dataset has the required variables to be passed in the macro keyword parameters.
- ▶ As we can see in the macro call, all the keyword parameters has variables that we can expect within the ADAE dataset except for the ROW variable.
- ▶ We followed the below derivation for ROW within the macro

```
proc sort data=adamdata.adae out=adaecall2(keep=aesoc aedecod) nodupkey;  
    by aesoc aedecod;  
    where saffl='Y' and aphasen=3;  
run;  
data adaecallall;  
    set adaecall2;  
    by aesoc;  
    row=_n_;  
run;
```

%coverage macro keyword parameters

Name	Required	Description	Valid Values
whr	Y	Subset to select required records from ADAE	Any valid analysis flag for subset
row	Y	Unique row number per SOC & PT	Derived ROW variable
soc	Y	SOC variable from ADAE	AESOC
pt	Y	PT variable from ADAE	AEDECOD
subset	N	Further subset condition at proc gemod level	Any valid WHERE condition

Calling the %convergence macro

```
data adaecall1;  
    set adaecall2;  
    by aesoc;  
    row=_n_;  
  
run;  
  
proc sort data=adaecall1 nodupkey;  
by aesoc aedecod;  
  
run;  
  
data _null_;  
set ADAECALLALL;  
  
call execute('%convergence(whr=%nrstr(anl07fl="Y" and  
aesoc='||quote(strip(aesoc))||'),row='||row||',  
soc='||quote(aesoc)||',pt='||quote(aedecod)||',subset=%nrstr());');  
  
run;
```

Calling the %convergence macro

- ▶ We get a separate convergence dataset for each SOC, PT for OR, RR and RD.
- ▶ We need to append all those individual datasets to one dataset.
- ▶ When we do so, we see the dataset as shown in the next slide

Convergence dataset

aesoc	aedecod	Status	Reason	stats	row
Gastrointestinal disorders		0	Algorithm converged.	OR	52
Gastrointestinal disorders		0	Algorithm converged.	RD	52
Gastrointestinal disorders		0	Algorithm converged.	RR	52
Gastrointestinal disorders	Colitis	0	Algorithm converged.	OR	69
Gastrointestinal disorders	Colitis	2	WARNING: The relative Hessian convergence criterion of 41.306071915 is greater than the limit of 0.0001. The convergence is questionable.	RD	69
Gastrointestinal disorders	Colitis	0	Algorithm converged.	RR	69
Gastrointestinal disorders	Large intestine perforation	0	Algorithm converged.	OR	96
Gastrointestinal disorders	Large intestine perforation	3	ERROR: The mean parameter is either invalid or at a limit of its range for some observations.	RD	96
Gastrointestinal disorders	Large intestine perforation	0	Algorithm converged.	RR	96
Gastrointestinal disorders	Rectal fissure	0	Algorithm converged.	OR	110
Gastrointestinal disorders	Rectal fissure	3	ERROR: The mean parameter is either invalid or at a limit of its range for some observations.	RD	110
Gastrointestinal disorders	Rectal fissure	0	Algorithm converged.	RR	110

Convergence Status

- ▶ As per the dataset we can see the numeric STATUS variable with values as 0,1,2 and 3 and a character column named Reason.
 - ▶ 0: converged; everything seemed fine
 - ▶ 1: converged, but there was some minor problem or a reason to question the results
 - ▶ 2: the iteration limit was reached without convergence, but everything seemed fine
 - ▶ 3: an error prevented further iteration

Convergence Status

- ▶ The model in genmod executes only when the convergence status is 0 and 2, when status is 1,3 or missing then it wont execute.
- ▶ Considering this we need to make the values 1 and 3 also missing, reason is that the main macro what we are going to use is programmed to execute the genmod procedure only when the status is not missing.
- ▶ If the status has 1 and 3 values then then genmod will execute and will result in error in the log which we want to avoid.
- ▶ Since the convergence status values are vertical per OR, RR and RD. we need to transpose them to get horizontal structure.

Transpose the Convergence Dataset for use in Main Macro

row	aesoc	aedecod	OR	RD	RR
52	Gastrointestinal disorders		0	0	0
69	Gastrointestinal disorders	Colitis	0	2	0
96	Gastrointestinal disorders	Large intestine perforation	0		0
110	Gastrointestinal disorders	Rectal fissure	0		0

%or_rr_rd macro to generate the output

- ▶ %or_rr_rd macro to create the final output with OR, RR and RD per every SOC and PT within the given data.
- ▶ It uses the macro parameters values of OR, RR and RD to conditionally execute the genmod procedure. If the macro parameter values of RD, OR or RR are missing then genmod will not execute, if they are not missing then genmod will execute.
- ▶ Example, a typical macro call to create the or_rr_rd data set will look like this

```
%or_rr_rd(whr=anl07fl="Y",  
          row=row,  
          soc=aesoc,  
          pt=aedecod,  
          rd=rd  
          or=or  
          rr=rr);
```

%or_rr_rd macro keyword parameters

Name	Required	Description	Valid Values
whr	Y	Subset to select required records from ADAE	Any valid analysis flag for subset
row	Y	Unique row number per SOC & PT	Derived ROW variable
soc	Y	SOC variable from ADAE	AESOC
pt	Y	PT variable from ADAE	AEDECOD
rd	Y	RD status variable from convergence dataset	RD
or	Y	OR status variable from convergence dataset	OR
rr	Y	RR status variable from convergence dataset	RR

Calling the %or_rr_rd macro

- ▶ Trans dataset used here is the transposed convergence dataset for use in %or_rr_rd macro

```
data _null_;  
set trans;  
  
call execute('%or_rr_rd(whr=%nrstr(&anl13 and  
aesoc='||quote(strip(aesoc))||'),row='||row||',soc='||quote(strip(aesoc))||'  
,pt='||quote(strip(aedecod))||',rd='||rd||',or='||or||',rr='||rr||');');  
  
run;
```

Final Output

TABLE 1

Analysis of Proportion of Subjects with Severe Adverse Events (Maximum Grade 3 or 4)

- by SOC and Preferred Term

System Organ Class Preferred Term	TRT 1 (N=284)	TRT 2 (N=285)	OR (95%CI)	RD (95%CI)	RR (95%CI)
Gastrointestinal disorders					
Any event	9 (3%)	4 (1%)	2.29 (0.69, 7.52)	1.76 (-0.69, 4.23)	2.25 (0.70, 7.22)
Colitis	2 (<1%)	2 (<1%)	1.00 (0.13, 7.14)	<0.00 (-1.38, 1.38)	1.00 (0.14, 7.05)
Large intestine perforation	3 (1%)	0	>999 (>999, >999)	NC	>999 (>999, >999)
Rectal fissure	0	1 (<1%)	<0.00 (<0.00, -)	NC	<0.00 (<0.00, -)

Note: OR = Odds Ratio; RD = Risk Difference (percentages); RR = Relative Risk. RD, OR and RR are obtained from genmod models (link = identity, logit or log, respectively) with no covariate adjustment. NC = Not Calculable. Zero counts for AEs in either treatment group may lead to unreliable statistical estimates.

References

- ▶ Proper Estimation of Relative Risk Using PROC GENMOD in Population Studies. Retrieved from [81_Paper.pdf \(lexjansen.com\)](#)
- ▶ SAS Documentation on Convergence Status. Retrieved from [SAS Help Center: Convergence Status](#)
- ▶ SAS Blog on Call Execute. Retrieved from [CALL EXECUTE made easy for SAS data-driven programming - SAS Users](#)

Thank you

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