

Streamlining Complex Analysis: A SAS Macro for Marginal Structural Modeling

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AGENDA

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- SAS Macros: model_msm.sas
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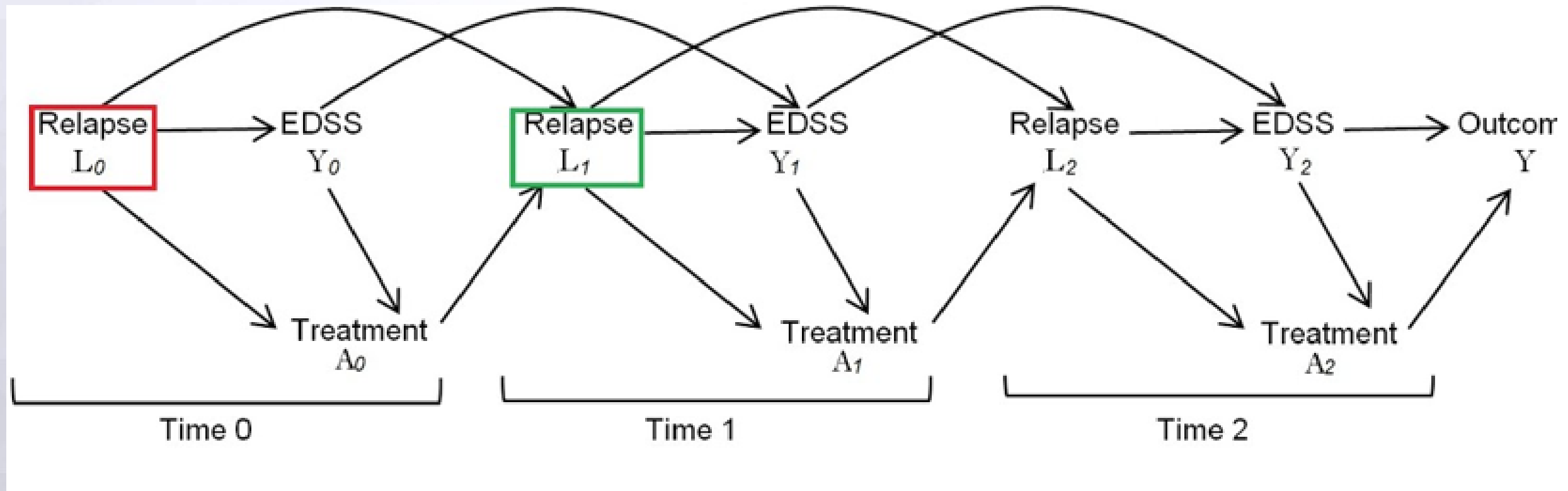


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INTRODUCTION



INTRODUCTION



OVERVIEW OF MARGINAL STRUCTURAL MODELS



OVERVIEW OF MARGINAL STRUCTURAL MODELS

- The general MSM formula for treatment effect estimation is:

$$E[Y(t)] = \beta_0 + \beta_1 t + \epsilon$$

where $Y(t)$ is the expected outcome at time t . The weights are computed based on treatment and confounder history to balance the pseudo-population.

- Time-varying confounders that are affected by prior treatments can create bias if handled using conventional regression models. MSMs use Inverse Probability Weighting (IPW) of treatment to create a pseudo-population in which treatment assignment is independent of measured confounders, ensuring unbiased causal effect estimates.
- To simplify the implementation of MSM in clinical research, we introduce a SAS macro, `Model_MSM.sas`, specifically designed to handle the complex data structures associated with longitudinal clinical trials.

OVERVIEW OF MARGINAL STRUCTURAL MODELS

Time	Cofounder 1	Cofounder 2
1	12	27
2	11	x
3	11	56
4	15	37
5	10	31
6	18	40
7	15	x
...	...	...



Time	Propensity Score	IPW
1	0.22	5
2	0.11	4
3	0.11	4
4	0.23	6
5	0.09	3
6	0.66	11
7	0.75	13
...	...	...

SAS MACROS: MODEL_MSM.SAS



SAS MACROS: MODEL_MSM.SAS

- **/* Step 1: Sort data by subject ID and time */**

```
proc sort data=&data;  
  by &id Time;  
run;
```

- **/* Step 2: Calculate inverse probability weights (IPW) */**

```
proc logistic data=&data;  
  class &treatment / param=ref;  
  model &treatment = &covariates / link=logit;  
  output out=weight_data p=prob;  
run;
```

```
data weight_data;  
  set weight_data;  
  ipw = 1 / prob; /* Calculate the inverse probability weight */  
run;
```

SAS MACROS: MODEL_MSM.SAS

- **/* Step 3: Apply weights in the MSM estimation */**

```
proc genmod data=weight_data;  
  class &id;  
  model &outcome = &treatment / dist=normal;  
  weight ipw; /* Use the calculated IPWs */  
  repeated subject=&id / type=ind; /* Account for repeated measures */  
  ods output ParameterEstimates=msm_results;  
run;
```

- **/* Step 4: Display the model results */**

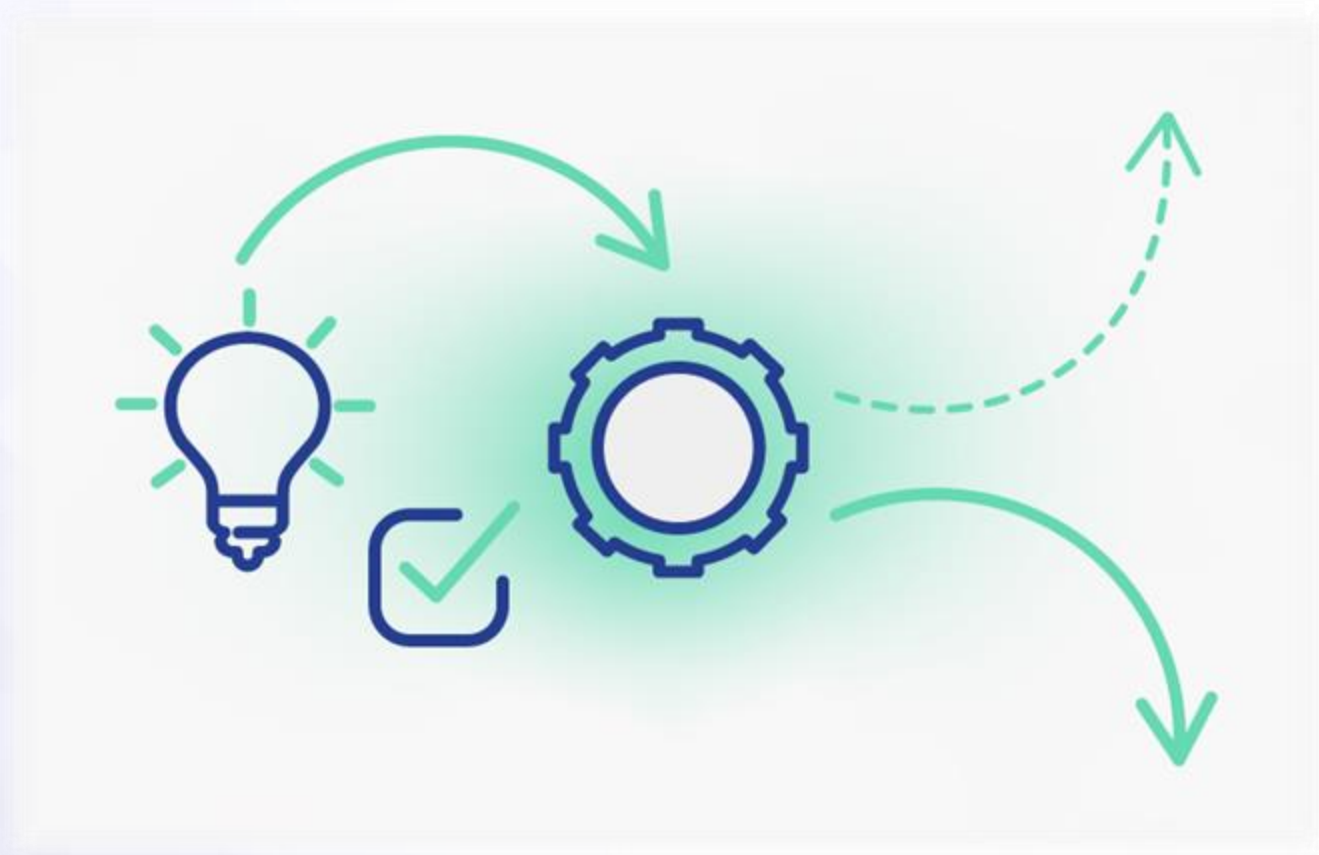
```
proc print data=msm_results;  
  var Parameter Estimate StdErr ProbZ;  
  title "MSM Parameter Estimates";  
run;  
%mend Model_MSM;
```

SAS MACROS: MODEL_MSM.SAS

- **/* Step 5: Check weight diagnostics */**

```
proc univariate data=weight_data;  
  var ipw;  
  title "Weight Diagnostics";  
run;  
%mend Model_MSM;
```

IMPLEMENTING THE SAS MACROS FOR MSM ANALYSIS



IMPLEMENTING THE SAS MACROS FOR MSM ANALYSIS

- The Model_MSM.sas macro simplifies MSM analysis by automating weight calculation, model estimation, and result reporting.
- Input Data Requirements:
 - Longitudinal data structure with repeated observations per patient.
 - Columns for treatment indicators, outcome variables, and time-varying covariates.
- Macro key Parameters:
 - data=: Name of the input dataset.
 - id=: Unique subject identifier.
 - treatment=: Treatment variable.
 - outcome=: Outcome variable of interest.
 - covariates=: List of time-varying confounders.
- Example SAS Code Using the Macro: `%include 'Model_MSM.sas'; /* Load the macro */`

IMPLEMENTING THE SAS MACROS FOR MSM ANALYSIS

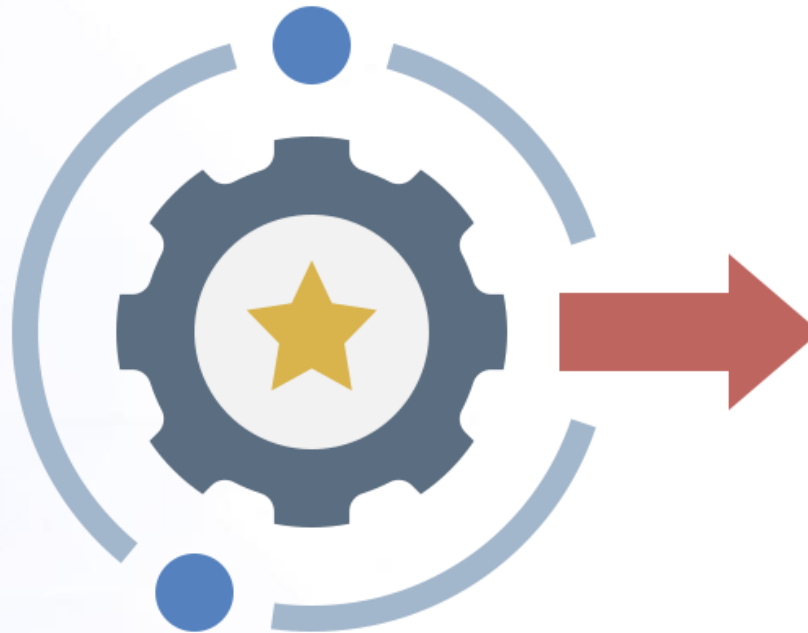
- **/* Step 1: Prepare the dataset */**

```
data trial_data;  
  input ID Time Treatment Outcome Age BP;  
  datalines;  
  1 1 0 5 50 120  
  1 2 1 6 51 122  
  2 1 1 4 60 130  
  2 2 0 3 61 135  
;  
run;
```

- **/* Step 2: Run the Model_MSM macro */**

```
%Model_MSM(  
  data=trial_data,  
  id=ID,  
  treatment=Treatment,  
  outcome=Outcome,  
  covariates=Age BP  
);
```

OUTPUT AND INTERPRETATION



OUTPUT AND INTERPRETATION

- The output generated by the Model_MSM.sas macro includes:
 - Descriptive statistics for the weighted population
 - Weight diagnostics to ensure the stability of IPW
 - Model estimation results with coefficients and confidence intervals
- The results show a statistically significant treatment effect ($p = 0.03$), with an estimated effect size of 0.65. The macro ensures that the estimated treatment effect is unbiased by properly accounting for time-varying confounders.

```
• Inverse Probability Weights
  Summary:
• -----
• Minimum Weight: 0.8
• Maximum Weight: 3.5

• Estimated Treatment Effect:
• -----
• Estimate StdErr p-value
• 0.65    0.12    0.03
```

MORE COMPLEX MACRO EXAMPLE FOR MSM



MORE COMPLEX MACRO EXAMPLE FOR MSM

******* SECTION 1 - Continuous outcome and continuous treatment*****;**

```
%macro
```

```
section1(indata=,outnum=,outcome=,prevout=,outchange=,imissvis=,dose=,construct=,  
plotwgts=0,plotout=0,checkcov=0,covtype=);
```

Options in the second row of the macro allow the user to indicate whether to plot the weights

- **Sorting and Initial Data Inspection**

```
proc sort data=&indata out=msm;  
by usubjid visitnum;  
run;
```

MORE COMPLEX MACRO EXAMPLE FOR MSM

- **Look at the amount of missing data for variables needed for the weighting models and analysis, including all dosing data**

```
proc means data=formsm nmiss;  
class visitnum;  
var age sex race medscat bmicat;  
run;
```

- **Obtaining Treatment Selection Weights**

```
ods output parameterestimates=nbparms;  
proc genmod data=formsm;  
model outcome= / dist=normal;  
output out=nbpreds p=nbpreds;  
run;
```

MORE COMPLEX MACRO EXAMPLE FOR MSM

- **Calculate densities and weights**

```
data &outd;  
merge &pd &pm;  
by temp;  
&densv=pdf('normal',outcome,&pd,ste);
```

- **Obtain baseline denominator densities**

```
proc genmod data=formsm;  
class sex race(ref='Caucasian or White');  
model outcome=age sex race  
&outcome / dist=normal;  
where visitnum=0;  
output out=dbpreds p=dbpreds;
```

MORE COMPLEX MACRO EXAMPLE FOR MSM

- **Obtain ratio of baseline numerator and denominator densities**

```
data blratio;  
merge predicts1 predicts2;  
by usubjid;  
rdens=dnum/dden;  
keep usubjid visitnum rdens;  
run;
```

MORE COMPLEX MACRO EXAMPLE FOR MSM

- Obtain cumulative product of ratio of densities across all visits

```
data trtwgts;  
set trtwgts;  
by usubjid visitnum;  
retain trtweight;  
if first.usubjid then trtweight=rdens;  
else trtweight=rdens*trtweight;  
run;
```

MORE COMPLEX MACRO EXAMPLE FOR MSM

- Obtain post-baseline numerator non-missing data probabilities

```
proc logistic data=formsm;  
class visitnum;  
model missvisit=visitnum prevasd;  
where visitnum ne 0;  
output out=nppreds (keep=usubjid visitnum npreds) p=npreds;  
run;
```

MORE COMPLEX MACRO EXAMPLE FOR MSM

- **Obtain final stabilized weights**

```
data finwgts1;  
merge trtwgts misswgts;  
by usubjid visitnum;  
stabwt=trtweight*missweight;  
run;
```

- **Plot weights**

```
proc sgplot data=finwgts;  
  vbox stabwt / category=visitnum;  
  where visitnum > 0;  
run;
```

MORE COMPLEX MACRO EXAMPLE FOR MSM

- **Run weighted repeated measures analysis**

```
proc means data=formodel nmiss;  
class visitnum;  
var &outchange stabwt &outcome &prevout;  
run;
```

- **Plot distribution of outcome variable**

```
proc univariate data=formodel;  
var &outchange;  
histogram &outchange;  
run;
```

MORE COMPLEX MACRO EXAMPLE FOR MSM

- **Run final model**

```
ods output geeempppest=parms estimates=estimates type3=type3;  
proc genmod data=formodel;  
class visitnum usubjid;  
weight stabwt;  
model &outchange = visitnum visitnum*&dose / dist=normal link=id  
type3;  
repeated subject=usubjid / type=&corstruct;  
estimate 'Dose effect at 3 Months' visitnum*&dose 0 0 0 5;  
estimate 'Dose effect at 6 Months' visitnum*&dose 0 0 0 0 0 0 5;  
run;
```

SUMMARY & CONCLUSION



SUMMARY & CONCLUSION



- Marginal Structural Models provide a powerful framework for estimating causal effects in the presence of time-varying confounders, making them particularly suitable for longitudinal clinical trials.
- The Model_MSM.sas macro simplifies the implementation of MSMs, allowing researchers to focus on interpreting results rather than the technical complexities of the methodology. With this macro, clinical trial data can be efficiently analyzed, leading to more reliable and interpretable findings that improve decision-making in healthcare research.



THANK YOU FOR YOUR ATTENTION
Q&A

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