

```

data epileptic_w;
input ID TRT Age C0 C1 C2 C3 C4;
datalines;
      1      0      31      11      5      3      3      3
      2      0      30      11      3      5      3      3
.....
     59      1      37      12      1      4      3      2
;
run;

```

## GEE vs GLMM

- **GEE is like studying all patients in a hospital and saying, "On average, this new epilepsy medication reduces seizure rates by 20%."** It gives a **broad, public health-focused conclusion** without worrying about individual differences.
- **GLMM is like a doctor adjusting a patient's treatment plan based on their unique seizure patterns.** Some patients might have **higher baseline seizure rates** than others, and GLMM accounts for these individual differences.

## Interpretation of Treatment Effects

- **Using GEE:**
  - The estimated treatment effect represents the **average reduction in seizure counts across all patients.**
  - Example interpretation: *"On average, patients taking the new medication experience 20% fewer seizures compared to the control group."*
  - This is useful if we care about **overall public health impact** rather than individual predictions.
- **Using GLMM:**
  - The treatment effect accounts for **individual differences in seizure frequency** (some patients may have naturally higher or lower seizure rates).
  - Example interpretation: *"For a given patient, the medication reduces their expected seizure count by 20% compared to their untreated seizure count."*
  - This is useful if we want **individualized predictions** (e.g., estimating how a specific patient might respond).

```

data epileptic;
set epileptic_w;
array AC(1:5) C0-C4;
array Aweek(1:5) (0 2 4 6 8);
do i=1 to 5;
  Count = AC[i];
  week = Aweek[i];
  L_per = log(2);
  if i eq 1 then L_per=log(8);
  output;
end;

```

```

drop C0-C4 Aweek1 - Aweek5 i;
run;

data epileptic;
set epileptic;
    rate = Count/exp(L_per);
    l_count = log(Count+1);
    l_rate = log((Count+1)/exp(L_per));
run;

proc print data=epileptic (obs=10);
run;

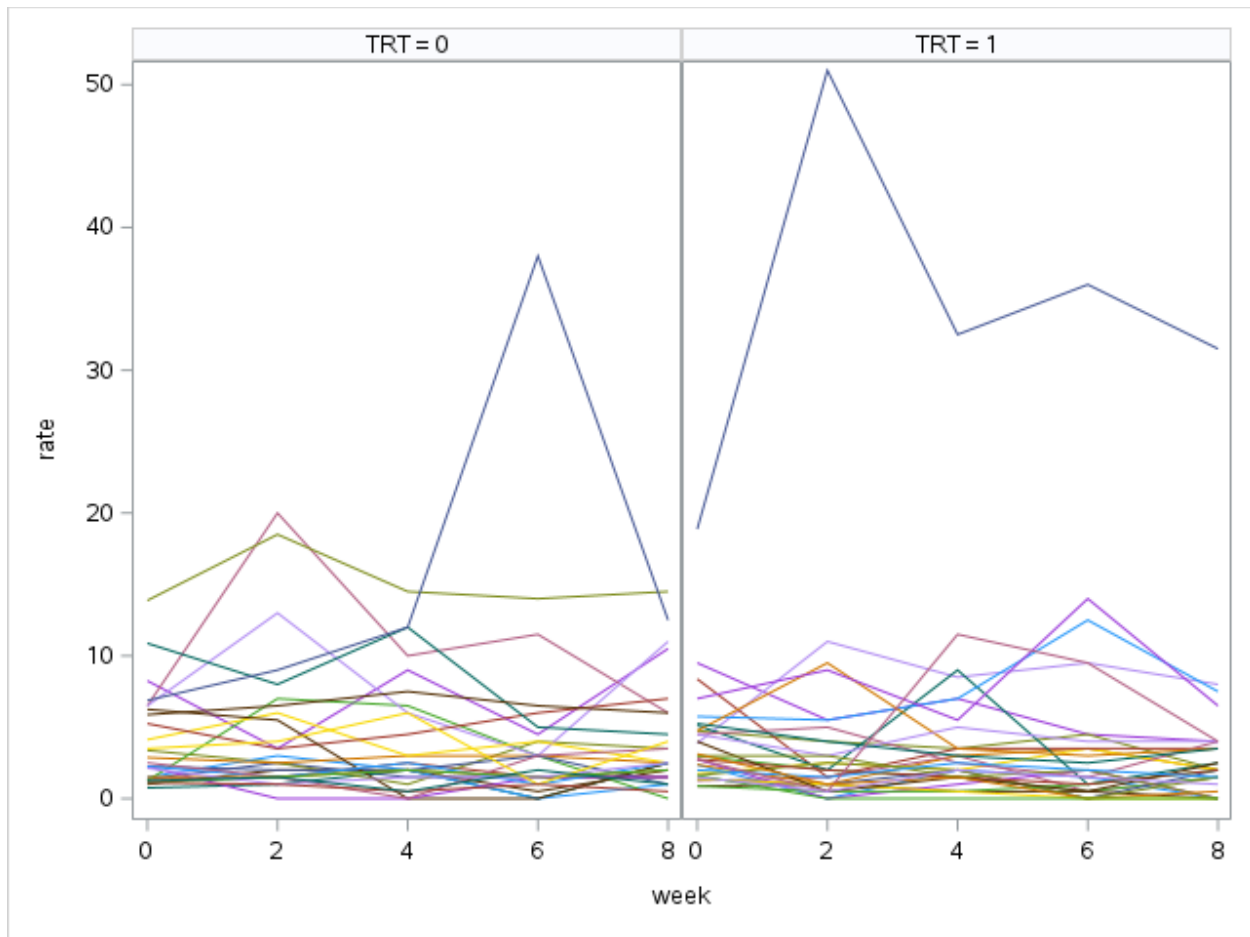
```

Obs	ID	TRT	Age	Count	week	L_per	rate	l_count	l_rate
1	1	0	31	11	0	2.07944	1.375	2.48491	0.40547
2	1	0	31	5	2	0.69315	2.500	1.79176	1.09861
3	1	0	31	3	4	0.69315	1.500	1.38629	0.69315
4	1	0	31	3	6	0.69315	1.500	1.38629	0.69315
5	1	0	31	3	8	0.69315	1.500	1.38629	0.69315
6	2	0	30	11	0	2.07944	1.375	2.48491	0.40547
7	2	0	30	3	2	0.69315	1.500	1.38629	0.69315
8	2	0	30	5	4	0.69315	2.500	1.79176	1.09861
9	2	0	30	3	6	0.69315	1.500	1.38629	0.69315
10	2	0	30	3	8	0.69315	1.500	1.38629	0.69315

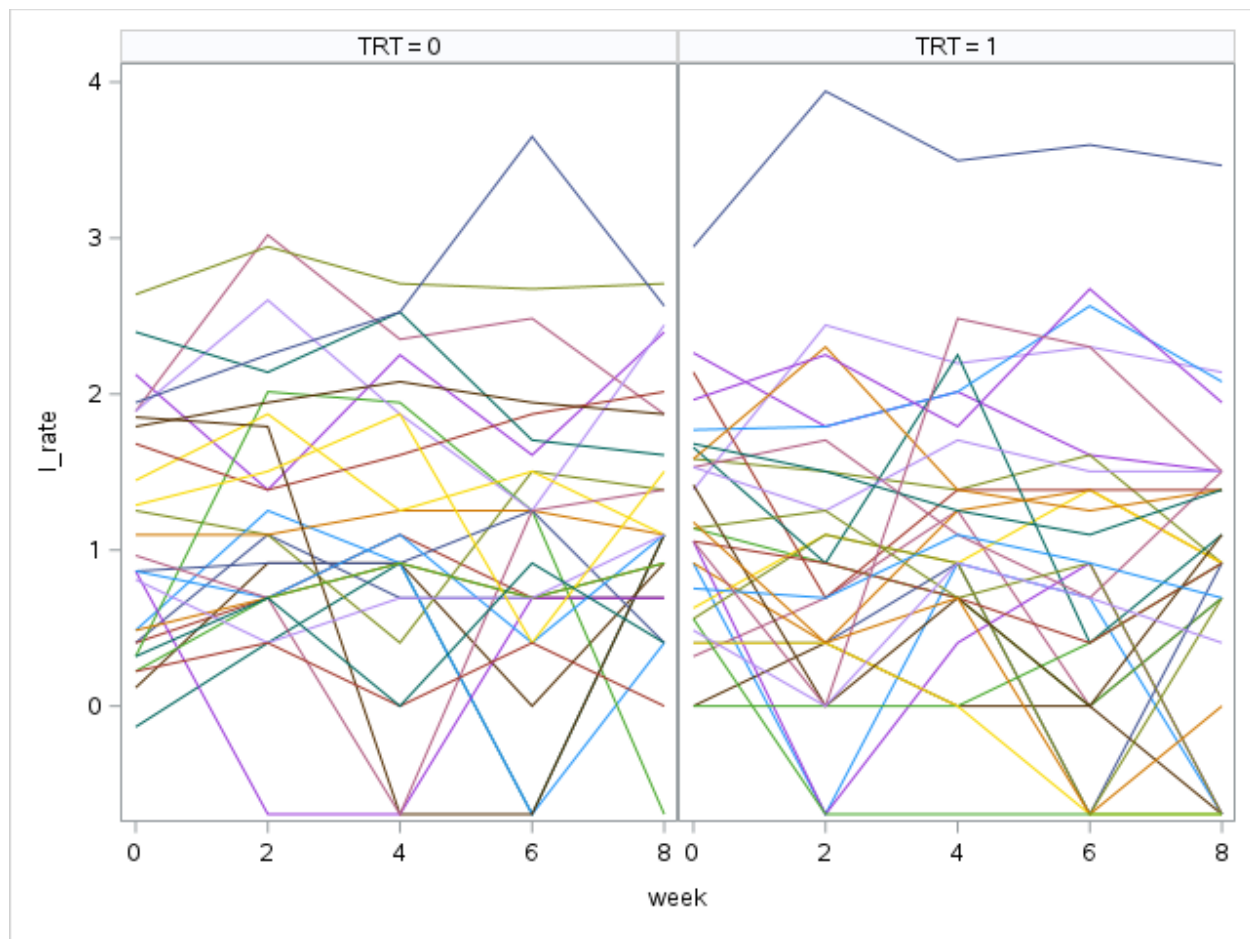
```

Proc SGpanel data = epileptic;
PanelBy TRT / columns=2;
series y=rate x=week / group =ID LineAttrs= (pattern=1 );
run;
quit;

```



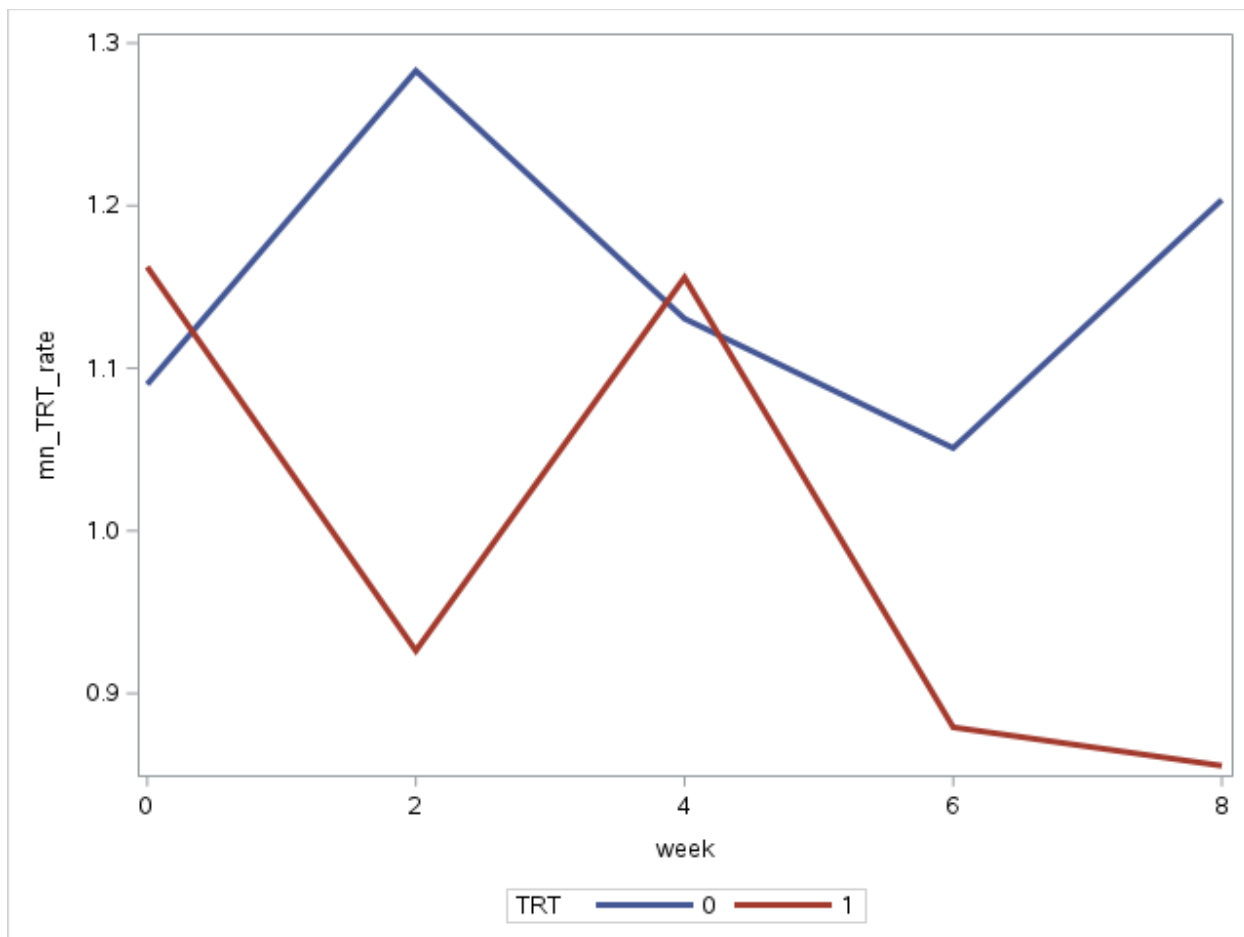
```
Proc SGpanel data = epileptic;
PanelBy TRT / columns=2;
series y=l_rate x=week / group =ID LineAttrs= (pattern=1 );
run;
quit;
```



```
proc sort data=epileptic;
by TRT week;
```

```
*Calculate the mean by week;
proc means mean data=epileptic noprint;
by TRT week;
var l_rate;
output out = MN_TRT_dat mean = mn_TRT_rate;
run;
```

```
*First, let's look at the mean by TRT group;
Proc SGplot data = MN_TRT_dat;
series x=week y=mn_TRT_rate / group =TRT LineAttrs= (pattern=1
thickness=3);
run;
```



```
proc gee data=epileptic;
class ID ;
model Count = TRT week TRT*week/d=poisson link=log offset=L_per
type3;
repeated subject=ID/type=exch corrw modelse covb ;
run;
quit;
```

#### The GEE Procedure

Model Information	
Data Set	WORK.EPILEPTIC
Distribution	Poisson
Link Function	Log
Dependent Variable	Count

Model Information			
Offset Variable		L_per	
Number of Observations Read		295	
Number of Observations Used		295	
Class Level Information			
Class	Levels	Values	
ID	59	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59	
Parameter Information			
Parameter	Effect		
Prm1	Intercept		
Prm2	TRT		
Prm3	week		
Prm4	TRT*week		
GEE Model Information			
Correlation Structure		Exchangeable	
Subject Effect		ID (59 levels)	
Number of Clusters		59	
Correlation Matrix Dimension		5	
Maximum Cluster Size		5	
Minimum Cluster Size		5	

Covariance Matrix (Model-Based)				
	Prm1	Prm2	Prm3	Prm4
Prm1	0.02404	-0.02404	0.001484	-0.001484
Prm2	-0.02404	0.04507	-0.001484	0.003109
Prm3	0.001484	-0.001484	0.0006504	-0.000650
Prm4	-0.001484	0.003109	-0.000650	0.001338

Covariance Matrix (Empirical)				
	Prm1	Prm2	Prm3	Prm4
Prm1	0.02749	-0.02749	0.0001172	-0.000117
Prm2	-0.02749	0.04355	-0.000117	0.0003482
Prm3	0.0001172	-0.000117	0.0005812	-0.000581
Prm4	-0.000117	0.0003482	-0.000581	0.0008272

Working Correlation Matrix					
	Obs 1	Obs 2	Obs 3	Obs 4	Obs 5
Obs 1	1.0000	0.7781	0.7781	0.7781	0.7781
Obs 2	0.7781	1.0000	0.7781	0.7781	0.7781
Obs 3	0.7781	0.7781	1.0000	0.7781	0.7781
Obs 4	0.7781	0.7781	0.7781	1.0000	0.7781
Obs 5	0.7781	0.7781	0.7781	0.7781	1.0000

Exchangeable Working Correlation	
Correlation	0.7781

GEE Fit Criteria	
QIC	-581.1965
QICu	-581.7413

Parameter Estimates for Response Model						
with Empirical Standard Error Estimates						
Parameter	Estimate	Standard Error	95% Confidence Limits		Z	Pr >  Z
Intercept	1.2901	0.1658	0.9651	1.6150	7.78	<.0001
TRT	0.0378	0.2087	-0.3712	0.4468	0.18	0.8563
week	-0.0009	0.0241	-0.0481	0.0464	-0.04	0.9708
TRT*week	-0.0188	0.0288	-0.0751	0.0376	-0.65	0.5143

Parameter Estimates for Response Model						
with Model-Based Standard Error Estimates						
Parameter	Estimate	Standard Error	95% Confidence Limits		Z	Pr >  Z
Intercept	1.2901	0.1550	0.9862	1.5939	8.32	<.0001
TRT	0.0378	0.2123	-0.3783	0.4539	0.18	0.8587
week	-0.0009	0.0255	-0.0509	0.0491	-0.03	0.9724
TRT*week	-0.0188	0.0366	-0.0905	0.0529	-0.51	0.6081

Score Statistics For Type 3 GEE Analysis			
Source	DF	Chi-Square	Pr > ChiSq
TRT	1	0.03	0.8549
week	1	0.00	0.9680
TRT*week	1	0.46	0.4967



### Interpretation of interaction

*Every additional week, the average seizure rate in the treatment group is multiplied by 0.9814 (or reduced by 1.86%) relative to the average seizure rate control group.*

### Interpretation of main effects

*At the beginning of the study (week 0), the average seizure rate in the treatment group is 1.0385 times (or 3.85% higher than) the control group.*

*In the control group, each additional week the average seizure rate is multiplied by 0.9991 (or decreases by 0.09%).*

```
proc gee data=epileptic;
class ID week (ref = '0');
model Count = TRT week TRT*week/d=poisson link=log offset=L_per
type3;
repeated subject=ID/type=exch corrw modelse covb ;
run;
quit;
```

GEE Fit Criteria	
QIC	-654.5784
QICu	-653.6516

Score Statistics For Type 3 GEE Analysis			
Source	DF	Chi-Square	Pr > ChiSq
TRT	1	0.03	0.8534
week	4	1.64	0.8012
TRT*week	4	1.80	0.7734

```
proc gee data=epileptic;
class ID ;
model Count = TRT week TRT*week/d=poisson link=log offset=L_per
type3;
repeated subject=ID/type=un corrw modelse covb ;
run;
quit;
```

Parameter Estimates for Response Model						
with Empirical Standard Error Estimates						
Parameter	Estimate	Standard Error	95% Confidence Limits		Z	Pr >  Z
Intercept	1.1074	0.3148	0.4904	1.7243	3.52	0.0004
TRT	0.1718	0.4013	-0.6148	0.9583	0.43	0.6687
week	-0.0170	0.0658	-0.1460	0.1119	-0.26	0.7956
TRT*week	-0.0031	0.0742	-0.1486	0.1423	-0.04	0.9663

```
proc gee data=epileptic;
class ID ;
model Count = TRT week TRT*week/d=negbin link=log offset=L_per
type3;
repeated subject=ID/type=exch corrw modelse covb ;
run;
quit;
```

The GEE Procedure			
Model Information			
Data Set		WORK.EPILEPTIC	
Distribution		Negative Binomial	
Link Function		Log	
Dependent Variable		Count	
Offset Variable		L_per	
Number of Observations Read		295	
Number of Observations Used		295	



Covariance Matrix (Empirical)				
	Prm1	Prm2	Prm3	Prm4
Prm1	0.02748	-0.02748	-0.000386	0.0003865
Prm2	-0.02748	0.07472	0.0003865	0.001479
Prm3	-0.000386	0.0003865	0.0004222	-0.000422
Prm4	0.0003865	0.001479	-0.000422	0.0006613

Working Correlation Matrix					
	Obs 1	Obs 2	Obs 3	Obs 4	Obs 5
Obs 1	1.0000	0.7486	0.7486	0.7486	0.7486
Obs 2	0.7486	1.0000	0.7486	0.7486	0.7486
Obs 3	0.7486	0.7486	1.0000	0.7486	0.7486
Obs 4	0.7486	0.7486	0.7486	1.0000	0.7486
Obs 5	0.7486	0.7486	0.7486	0.7486	1.0000

Exchangeable Working Correlation	
Correlation	0.7486
GEE Fit Criteria	
QIC	-8251.4951
QICu	-8258.4515

Parameter Estimates for Response Model					
with Empirical Standard Error Estimates					
Parameter	Estimate	Standard Error	95% Confidence Limits		Z Pr >  Z
Intercept	1.4214	0.1658	1.0965	1.7463	8.57 <.0001

Parameter Estimates for Response Model						
with Empirical Standard Error Estimates						
Parameter	Estimate	Standard Error	95% Confidence Limits		Z	Pr >  Z
TRT	0.0183	0.2733	-0.5175	0.5540	0.07	0.9467
week	0.0009	0.0205	-0.0393	0.0412	0.05	0.9633
TRT*week	-0.0187	0.0257	-0.0691	0.0317	-0.73	0.4660
Parameter Estimates for Response Model						
with Model-Based Standard Error Estimates						
Parameter	Estimate	Standard Error	95% Confidence Limits		Z	Pr >  Z
Intercept	1.4214	0.2508	0.9300	1.9129	5.67	<.0001
TRT	0.0183	0.3459	-0.6596	0.6962	0.05	0.9579
week	0.0009	0.0212	-0.0406	0.0425	0.04	0.9645
TRT*week	-0.0187	0.0293	-0.0762	0.0387	-0.64	0.5224
Score Statistics For Type 3 GEE Analysis						
Source	DF	Chi-Square	Pr > ChiSq			
TRT	1	0.00	0.9477			
week	1	0.00	0.9644			
TRT*week	1	0.50	0.4779			