```
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;
```

(handwritten annotations: 4 8, arrows labeled 2, 2, 2, 2, "Offset")

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;
```

(handwritten annotation: Offset = log(per))

```
    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;
```

rate = $\frac{Count}{per}$

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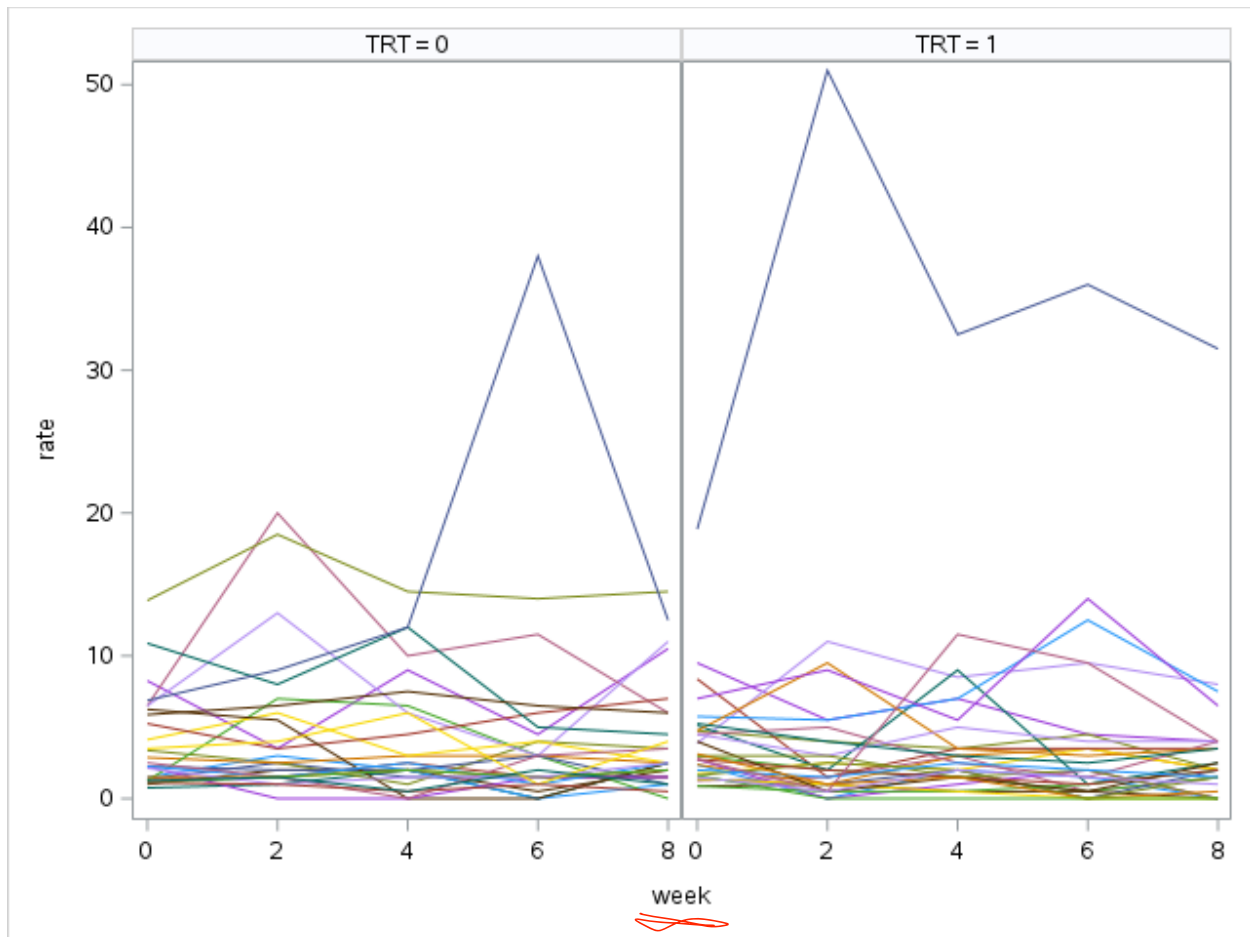
```
Proc SGpanel data = epileptic;
PanelBy TRT / columns=2;
series y=l_rate x=week / group =ID LineAttrs= (pattern=1 );
run;
quit;
```
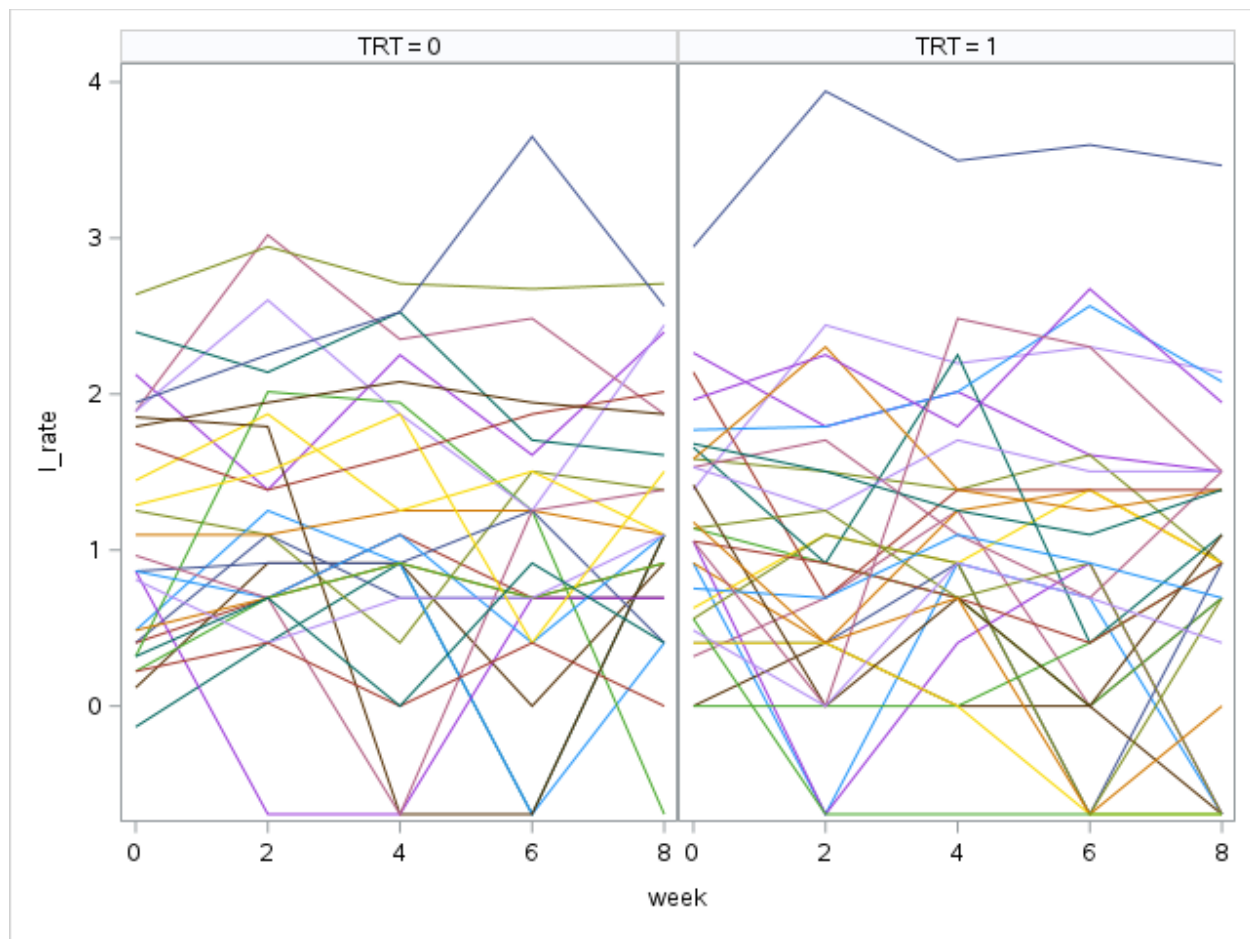
```
proc sort data=epileptic;
by TRT week;

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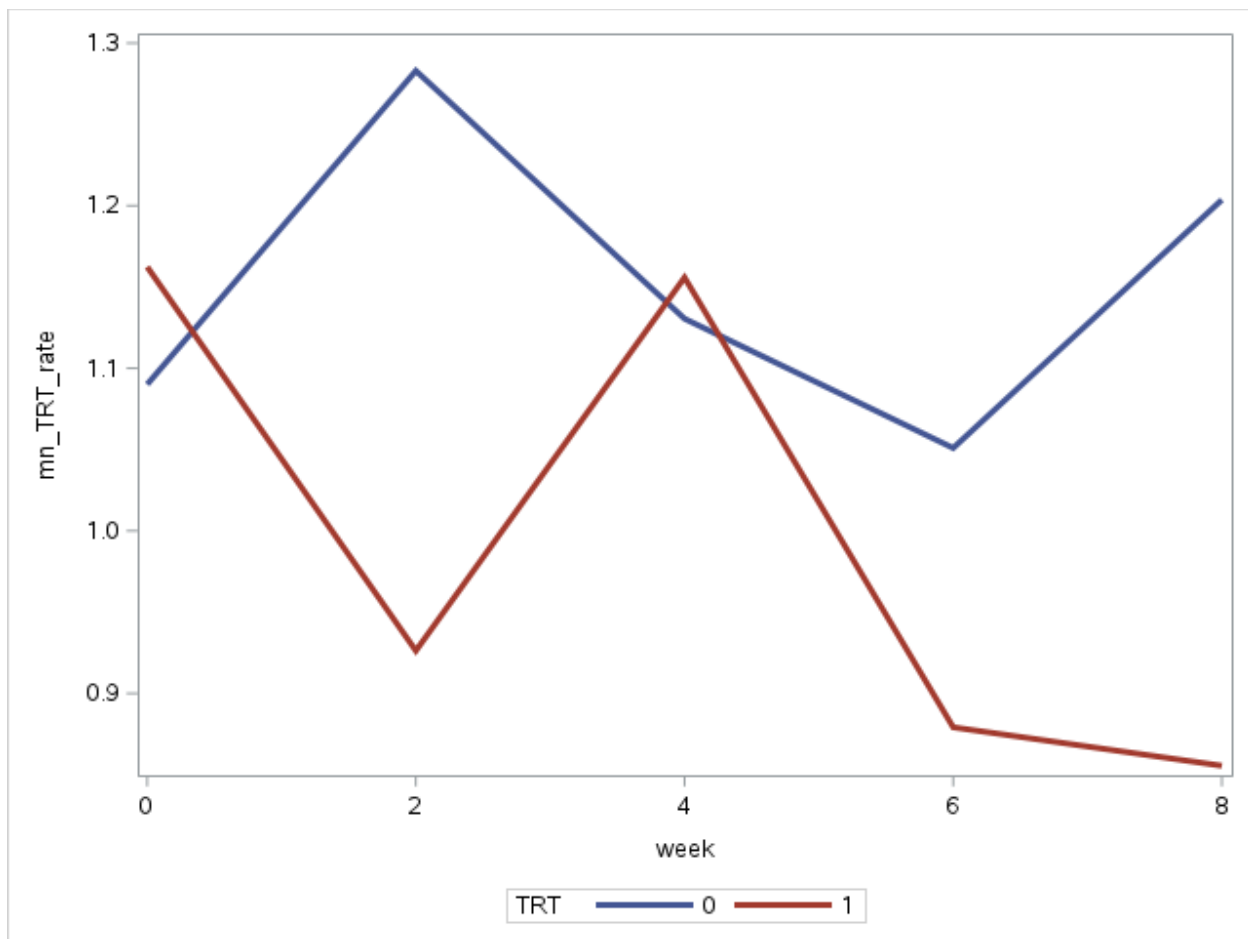
```
proc gee data=epileptic;
class ID ;
model Count = TRT week TRT*week/d=poisson link=log offset=L_per
type3;
repeated subject=ID/type=exch corrw modelse covb ;
run;
quit;
```

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%).

↳ per week

```
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

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	0.06288	-0.06288	-0.001524	0.001524
Prm2	-0.06288	0.11962	0.001524	-0.002855
Prm3	-0.001524	0.001524	0.0004494	-0.000449
Prm4	0.001524	-0.002855	-0.000449	0.0008587

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