

Example: The data are from a randomized, double-blind, parallel-group, multicenter study comparing two oral treatments (denoted A and B) for toe-nail infection. Patients were evaluated for the degree of onycholysis (the degree of separation of the nail plate from the nail-bed) at baseline (week 0) and at weeks 4, 8, 12, 24, 36, and 48 thereafter. The onycholysis outcome variable is binary (none or mild versus moderate or severe). The binary outcome was evaluated on 294 patients comprising a total of 1908 measurements.

```
data toenail;
input ID Response Treatment Month Visit;
rd_month = round(Month);
datalines;
1 1 1 0 1
1 1 1 0.8571428571 2
1 1 1 3.5357142857 3
1 0 1 4.5357142857 4
1 0 1 7.5357142857 5
1 0 1 10.035714286 6
1 0 1 13.071428571 7
2 0 0 0 1
.....
;
```

TRIM

```
proc sort data = toenail;
by treatment rd_month;
run;
```

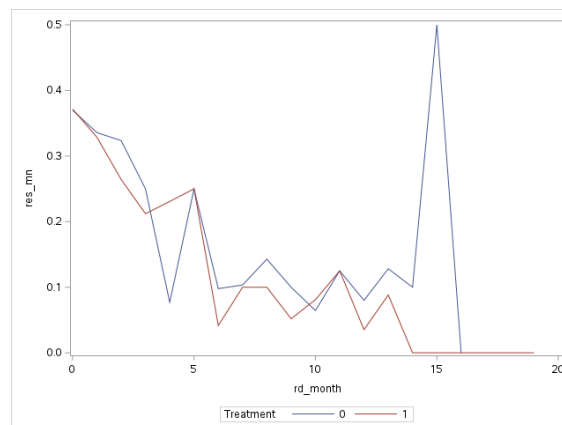
```
proc means data = toenail noprint;
by treatment rd_month;
var Response;
output out=mn_dat mean=res_mn;
run;
```

```
proc print data=mn_dat;
run;
```

Obs	Treatment	rd_month	_TYPE_	_FREQ_	res_mn
1	0	0	0	146	0.36986
2	0	1	0	137	0.33577
3	0	2	0	136	0.32353
4	0	3	0	124	0.25000
5	0	4	0	13	0.07692
6	0	5	0	4	0.25000
7	0	6	0	92	0.09783
8	0	7	0	29	0.10345
9	0	8	0	7	0.14286
10	0	9	0	80	0.10000
11	0	10	0	31	0.06452

Obs	Treatment	rd_month	_TYPE_	_FREQ_	res_mn
12	0	11	0	8	0.12500
13	0	12	0	75	0.08000
14	0	13	0	39	0.12821
15	0	14	0	10	0.10000
16	0	15	0	2	0.50000
17	0	16	0	4	0.00000
18	1	0	0	148	0.37162
19	1	1	0	146	0.32877
20	1	2	0	140	0.26429
21	1	3	0	132	0.21212
22	1	4	0	13	0.23077
23	1	5	0	4	0.25000
24	1	6	0	96	0.04167
25	1	7	0	30	0.10000
26	1	8	0	10	0.10000
27	1	9	0	77	0.05195
28	1	10	0	37	0.08108
29	1	11	0	8	0.12500
30	1	12	0	85	0.03529
31	1	13	0	34	0.08824
32	1	14	0	7	0.00000
33	1	15	0	2	0.00000
34	1	16	0	1	0.00000
35	1	19	0	1	0.00000

```
proc sgplot data=mn_dat;
series x = rd_month y = res_mn/ group=treatment;
run;
```



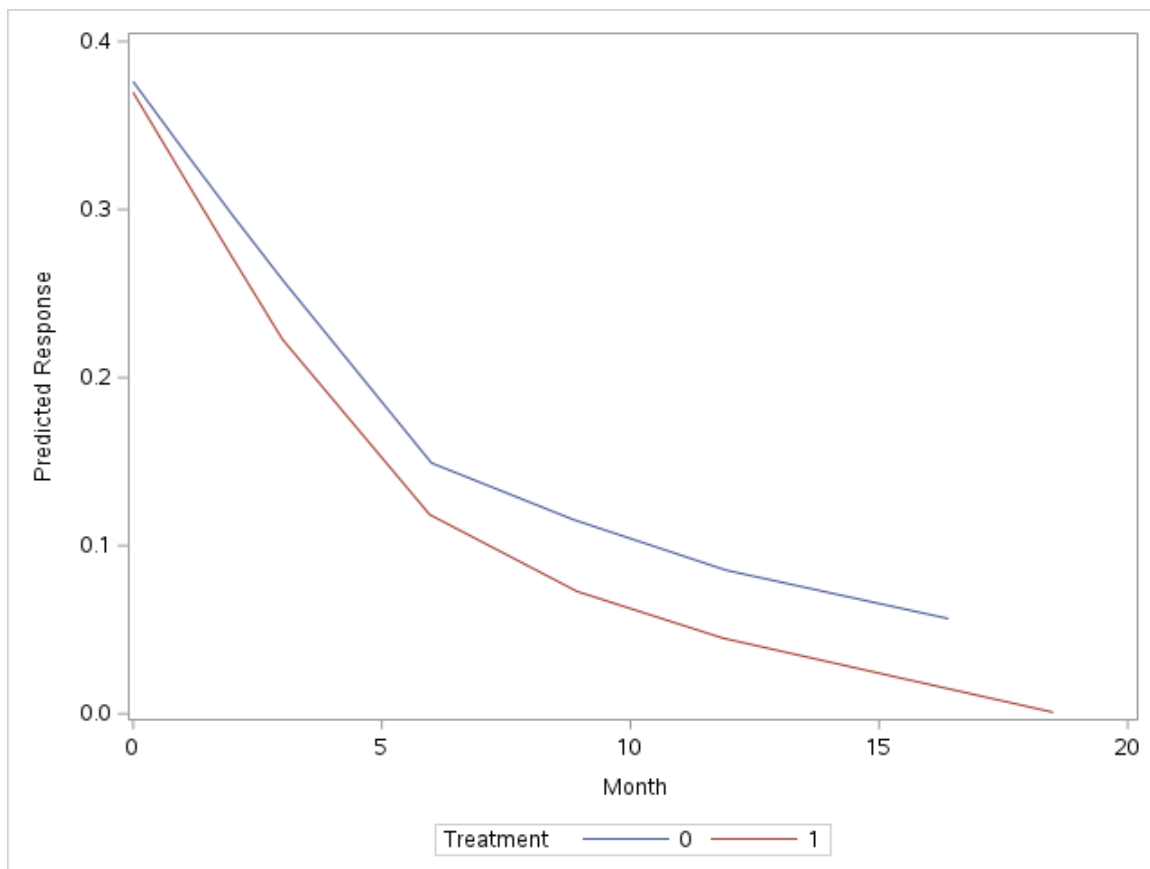
```

proc loess data=toenail plots=none;
  ods output outputstatistics=out_low;
  by treatment;
  model Response=Month;
run;

proc sort data=out_low;
  by treatment Month;
run;

proc sgplot data=out_low;
  series x=Month y=pred/ group = treatment;
run;

```

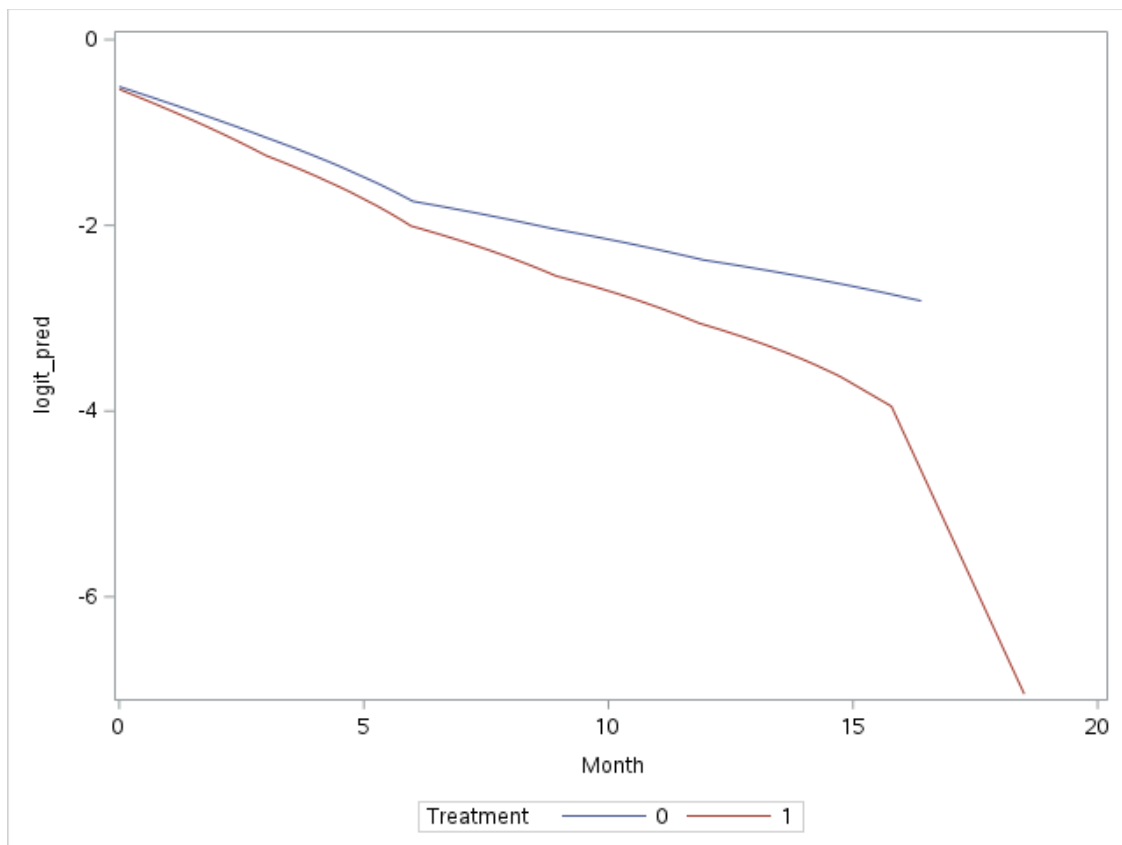


```

data out_low2;
set out_low;
logit_pred = log(pred/(1-pred));
run;

proc sgplot data=out_low2;
  series x=Month y=logit_pred/ group = treatment;
run;

```



```
proc glimmix data=toenail method=quad(qpoints=20);
class ID treatment;
model Response=Treatment Month Treatment*Month /dist=bin link=logit
solution;
random intercept /type=UN G Gcorr subject=ID;
run;
```

The GLIMMIX Procedure

Model Information	
Data Set	WORK.TOENAIL
Response Variable	Response
Response Distribution	Binomial
Link Function	Logit
Variance Function	Default

Model Information	
Variance Matrix Blocked By	ID
Estimation Technique	Maximum Likelihood
Likelihood Approximation	Gauss-Hermite Quadrature
Degrees of Freedom Method	Containment

Class Level Information		
Class	Levels	Values
ID	294	1 2 3 4 6 7 383
Treatment	2	0 1

Number of Observations Read	1908
Number of Observations Used	1908

Dimensions	
G-side Cov. Parameters	1
Columns in X	6
Columns in Z per Subject	1
Subjects (Blocks in V)	294
Max Obs per Subject	7

Optimization Information	
Optimization Technique	Dual Quasi-Newton
Parameters in Optimization	5
Lower Boundaries	1
Upper Boundaries	0

Optimization Information					
Fixed Effects			Not Profiled		
Starting From			GLM estimates		
Quadrature Points			20		
Iteration History					
Iteration	Restarts	Evaluations	Objective	Change	Max
0	0	4	1382.811832	.	760.0019
1	0	3	1360.0584047	22.75342732	354.5137
2	0	2	1346.5901737	13.46823101	216.5517
3	0	4	1311.8479066	34.74226708	104.2334
4	0	4	1300.4845975	11.36330908	64.07118
5	0	4	1266.4231807	34.06141680	36.71963
6	0	3	1253.002871	13.42030971	21.88316
7	0	3	1251.6637539	1.33911708	23.20562
8	0	3	1251.2528465	0.41090746	5.629866
9	0	3	1251.0146277	0.23821877	2.107496
10	0	3	1250.9244053	0.09022241	5.329818
11	0	2	1250.7762193	0.14818599	0.797992
12	0	3	1250.7515826	0.02463673	1.153387
13	0	3	1250.7506018	0.00098080	0.192758
14	0	3	1250.7505464	0.00005535	0.006712
15	0	3	1250.7505462	0.00000019	0.000682
Convergence criterion (GCONV=1E-8) satisfied.					

Fit Statistics	
-2 Log Likelihood	1250.75
AIC (smaller is better)	1260.75
AICC (smaller is better)	1260.78
BIC (smaller is better)	1279.17
CAIC (smaller is better)	1284.17
HQIC (smaller is better)	1268.13

Fit Statistics for Conditional Distribution	
-2 log L(Response r. effects)	630.87
Pearson Chi-Square	4331.92
Pearson Chi-Square / DF	2.27

Estimated G Matrix		
Effect	Row	Col1
Intercept	1	16.0297

Covariance Parameter Estimates			
Cov Parm	Subject	Estimate	Standard Error
UN(1,1)	ID	16.0297	3.0011

Solutions for Fixed Effects						
Effect	Treatment	Estimate	Standard	DF	t Value	Pr > t
Intercept		-1.7790	0.4456	292	-3.99	<.0001
Treatment	0	0.1608	0.5837	1612	0.28	0.7830
Treatment	1	0
Month		-0.5276	0.05614	1612	-9.40	<.0001
Month*Treatment	0	0.1367	0.06799	1612	2.01	0.0445
Month*Treatment	1	0

```
proc glimmix data=toenail method=quad(qpoints=20);
class ID treatment;
model Response=Treatment Month Treatment*Month /dist=bin link=logit
solution;
random intercept Month/type=UN G Gcorr subject=ID;
run;
```

The GLIMMIX Procedure

Model Information	
Data Set	WORK.TOENAIL
Response Variable	Response

Model Information	
Response Distribution	Binomial
Link Function	Logit
Variance Function	Default
Variance Matrix Blocked By	ID
Estimation Technique	Maximum Likelihood
Likelihood Approximation	Gauss-Hermite Quadrature
Degrees of Freedom Method	Containment

Class Level Information		
Class	Levels	Values
ID	294	1 2 3 4 6 7 9 383
Treatment	2	0 1

Number of Observations Read	1908
Number of Observations Used	1908

Dimensions	
G-side Cov. Parameters	3
Columns in X	6
Columns in Z per Subject	2
Subjects (Blocks in V)	294
Max Obs per Subject	7

Optimization Information	
Optimization Technique	Dual Quasi-Newton

Optimization Information					
Parameters in Optimization		7			
Lower Boundaries		2			
Upper Boundaries		0			
Fixed Effects		Not Profiled			
Starting From		GLM estimates			
Quadrature Points		20			
Iteration History					
Iteration	Restarts	Evaluations	Objective	Change	Max
0	0	4	1357.2654985	.	663.6751
1	0	5	1273.5404156	83.72508294	603.5629
2	0	3	1250.4812363	23.05917929	48.31572
3	0	2	1239.2396062	11.24163014	172.2946
4	0	2	1225.7780618	13.46154434	26.50946
5	0	4	1219.1122881	6.66577371	31.47332
6	0	4	1187.0563511	32.05593705	69.63307
7	0	2	1147.5214642	39.53488687	89.05815
8	0	2	1106.4960705	41.02539371	15.20876
9	0	3	1104.2147554	2.28131508	37.86331
10	0	2	1102.1667677	2.04798774	11.0414
11	0	3	1100.8565981	1.31016953	12.38747
12	0	3	1100.231008	0.62559013	10.07158
13	0	2	1099.70387	0.52713799	14.05279
14	0	2	1099.2255531	0.47831689	6.291872
15	0	4	1098.1906834	1.03486976	6.480524
16	0	3	1098.1100468	0.08063652	7.260189
17	0	2	1098.0881544	0.02189240	4.598288
18	0	4	1097.9730844	0.11507009	7.278862
19	0	4	1097.5948136	0.37827071	6.452527
20	0	2	1097.1305365	0.46427718	13.12123
21	0	4	1095.7207883	1.40974816	9.20452
22	0	3	1095.5910619	0.12972637	4.183606
23	0	3	1095.501975	0.08908693	2.010579

Iteration History					
Iteration	Restarts	Evaluations	Objective	Change	Max
24	0	2	1095.4509368	0.05103822	1.105105
25	0	4	1095.1917269	0.25920985	1.790633
26	0	3	1095.1452936	0.04643336	2.490579
27	0	2	1095.0980008	0.04729278	2.098409
28	0	4	1094.6892416	0.40875924	3.650669
29	0	2	1094.1974159	0.49182565	1.592913
30	0	3	1094.182318	0.01509796	1.4832
31	0	3	1094.180643	0.00167501	1.891713
32	0	4	1094.1695906	0.01105232	1.780044
33	0	4	1094.0512919	0.11829876	1.550915
34	0	3	1094.0427298	0.00856206	0.131013
35	0	3	1094.0425468	0.00018303	0.01737
36	0	3	1094.042538	0.00000874	0.000568
37	0	3	1094.042538	0.00000002	0.000113

Convergence criterion (GCONV=1E-8) satisfied.

Fit Statistics	
-2 Log Likelihood	1094.04
AIC (smaller is better)	1108.04
AICC (smaller is better)	1108.10
BIC (smaller is better)	1133.83
CAIC (smaller is better)	1140.83
HQIC (smaller is better)	1118.37

Fit Statistics for Conditional Distribution	
-2 log L(Response r. effects)	209.63
Pearson Chi-Square	157.07
Pearson Chi-Square / DF	0.08

Estimated G Matrix			
Effect	Row	Col1	Col2
Intercept	1	179.91	-13.4085
Month	2	-13.4085	2.1557

Estimated G Correlation Matrix			
Effect	Row	Col1	Col2
Intercept	1	1.0000	-0.6809
Month	2	-0.6809	1.0000

Covariance Parameter Estimates			
Cov Parm	Subject	Estimate	Standard Error
UN(1,1)	ID	179.91	51.2582
UN(2,1)	ID	-13.4085	4.3381
UN(2,2)	ID	2.1557	0.6291

Solutions for Fixed Effects						
Effect	Treatment	Estimate	Standard Error	DF	t Value	Pr > t
Intercept		-5.5757	1.4840	292	-3.76	0.0002
Treatment	0	0.2160	1.6621	1325	0.13	0.8966
Treatment	1	0
Month		-1.4701	0.3141	287	-4.68	<.0001
Month*Treatment	0	0.5754	0.2400	1325	2.40	0.0167
Month*Treatment	1	0

```
proc glimmix data=toenail method=quad(qpoints=20);
class ID treatment;
model Response=Treatment Month Treatment*Month Month*Month
Treatment*Month*Month/dist=bin link=logit solution;
random intercept Month/type=UN G Gcorr subject=ID;
run;
```

The GLIMMIX Procedure

Model Information				
Data Set			WORK.TOENAIL	
Response Variable			Response	
Response Distribution			Binomial	
Link Function			Logit	
Variance Function			Default	
Variance Matrix Blocked By			ID	
Estimation Technique			Maximum Likelihood	
Likelihood Approximation			Gauss-Hermite Quadrature	
Degrees of Freedom Method			Containment	
Class Level Information				
Class		Levels	Values	
ID		294	1 2 3 4 6 7383	
Treatment		2	0 1	
Number of Observations Read			1908	
Number of Observations Used			1908	
Dimensions				
G-side Cov. Parameters			3	

Dimensions	
Columns in X	9
Columns in Z per Subject	2
Subjects (Blocks in V)	294
Max Obs per Subject	7

Optimization Information	
Optimization Technique	Dual Quasi-Newton
Parameters in Optimization	9
Lower Boundaries	2
Upper Boundaries	0
Fixed Effects	Not Profiled
Starting From	GLM estimates
Quadrature Points	20

Iteration History					
Iteration	Restarts	Evaluations	Objective	Change	Max
0	0	4	1349.0996888	.	6887.951
1	0	5	1309.6625753	39.43711350	2775.242
2	0	4	1284.3319512	25.33062406	1684.391
3	0	3	1270.2980856	14.03386561	1155.441
4	0	2	1248.1134807	22.18460493	987.126
5	0	2	1241.2795609	6.83391982	671.7117
6	0	4	1223.0714383	18.20812253	395.9117
7	0	2	1215.6365366	7.43490176	1519.667
8	0	2	1203.1228054	12.51373114	704.0746
9	0	2	1184.4503158	18.67248969	57.78881
10	0	2	1157.8368027	26.61351301	384.9929
11	0	2	1131.7093405	26.12746229	361.7153
12	0	2	1119.2743167	12.43502380	326.2166
13	0	3	1116.7586526	2.51566407	207.7557

Iteration History					
Iteration	Restarts	Evaluations	Objective	Change	Max
14	0	2	1114.0124883	2.74616431	211.4221
15	0	2	1113.2399465	0.77254180	206.3449
16	0	4	1110.6946466	2.54529991	194.798
17	0	3	1109.5625143	1.13213222	85.41736
18	0	2	1107.9770686	1.58544577	91.82533
19	0	3	1107.3530798	0.62398874	30.8557
20	0	2	1107.1081906	0.24488921	189.276
21	0	4	1106.5738833	0.53430736	14.69111
22	0	2	1106.2350111	0.33887213	46.62949
23	0	2	1105.8142925	0.42071860	14.24222
24	0	2	1105.0976694	0.71662316	35.13131
25	0	3	1104.6646041	0.43306522	14.67025
26	0	3	1104.5358741	0.12873003	52.01641
27	0	4	1104.1682093	0.36766482	41.04924
28	0	3	1103.9810963	0.18711303	18.28475
29	0	2	1103.7543293	0.22676695	40.89876
30	0	3	1103.6655646	0.08876468	35.83084
31	0	3	1103.6096007	0.05596388	40.13425
32	0	4	1103.4736423	0.13595842	16.89848
33	0	4	1102.3441533	1.12948906	67.58993
34	0	2	1100.6404334	1.70371990	118.1592
35	0	3	1099.6003444	1.04008893	23.20402
36	0	5	1099.2599481	0.34039632	34.17144
37	0	3	1099.170154	0.08979412	40.32876
38	0	2	1099.0714631	0.09869085	38.89982
39	0	4	1098.8265031	0.24496002	35.36252
40	0	2	1098.6322386	0.19426457	30.27343
41	0	4	1098.2238525	0.40838604	92.55832
42	0	4	1095.2666835	2.95716905	27.54393
43	0	2	1091.6372564	3.62942709	201.0628
44	0	3	1089.5952929	2.04196348	41.20429
45	0	3	1089.1745021	0.42079076	31.70512
46	0	3	1089.0306963	0.14380588	14.23121
47	0	3	1089.0164576	0.01423870	4.437206
48	0	2	1088.9960089	0.02044869	7.404377
49	0	4	1088.9415123	0.05449658	11.6282

Iteration History					
Iteration	Restarts	Evaluations	Objective	Change	Max
50	0	4	1088.5490563	0.39245598	140.0475
51	0	4	1087.7975492	0.75150715	64.59582
52	0	3	1087.466678	0.33087115	13.68005
53	0	3	1087.4431032	0.02357483	5.759942
54	0	3	1087.4410662	0.00203703	0.176205
55	0	3	1087.441036	0.00003019	0.09476
56	0	3	1087.4410349	0.00000105	0.007995

Convergence criterion (GCONV=1E-8) satisfied.

Fit Statistics	
-2 Log Likelihood	1087.44
AIC (smaller is better)	1105.44
AICC (smaller is better)	1105.54
BIC (smaller is better)	1138.59
CAIC (smaller is better)	1147.59
HQIC (smaller is better)	1118.72

Fit Statistics for Conditional Distribution	
-2 log L(Response r. effects)	179.47
Pearson Chi-Square	128.33
Pearson Chi-Square / DF	0.07

Estimated G Matrix			
Effect	Row	Col1	Col2
Intercept	1	218.06	-17.4334
Month	2	-17.4334	3.5962

Estimated G Correlation Matrix			
Effect	Row	Col1	Col2
Intercept	1	1.0000	-0.6225
Month	2	-0.6225	1.0000

Covariance Parameter Estimates			
Cov Parm	Subject	Estimate	Standard Error
UN(1,1)	ID	218.06	60.4933
UN(2,1)	ID	-17.4334	5.4958
UN(2,2)	ID	3.5962	1.1940

Solutions for Fixed Effects						
Effect	Treatment	Estimate	Standard	DF	t Value	Pr > t
Intercept		-6.5412	1.5735	292	-4.16	<.0001
Treatment	0	0.5198	1.7881	1323	0.29	0.7713
Treatment	1	0
Month		-1.0655	0.3930	287	-2.71	0.0071
Month*Treatment	0	0.06090	0.4638	1323	0.13	0.8955
Month*Treatment	1	0
Month*Month		-0.09583	0.04372	1323	-2.19	0.0286
Month*Month*Treatmen	0	0.06982	0.04236	1323	1.65	0.0995
Month*Month*Treatmen	1	0