Criterion	GEE (Population-Averaged)	GLMM (Subject-Specific)
Goal	Understand the average effect of the treatment across all patients	Understand how treatment affects individuals differently
Correlation Handling	Uses a working correlation structure	Uses patient-specific random effects
Interpretation of Effects	Marginal (population-level)	Conditional (subject-specific)
When to Use	Policy decisions, public health impact	Personalized treatment decisions, individualized modeling
Computational Complexity	Easier to estimate, robust to correlation misspecification	More computationally intensive but captures individual variability

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.

Estimation

One thing to note with this data is that the parameter estimates markedly change with the number of quadrature nodes: **The following have a random intercepts and slopes**

Q=1 Quadrature Node which took T=1.4 seconds to run

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
UN(1,1)	**ID**	5864.32	1911.22
UN(2,1)	**ID**	-151.59	98.8156
UN(2,2)	**ID**	127.79	51.3348

Solutions for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	-12.3114	1.1700	292	-10.52	<.0001
Treatment	-0.1591	1.5153	1325	-0.10	0.9164
Month	-10.8162	1.8568	287	-5.83	<.0001
Treatment*Month	-1.4697	1.2562	1325	-1.17	0.2422

Q=5 and T=4.18 seconds

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
UN(1,1)	ID	291.24	101.17
UN(2,1)	ID	-21.3732	8.3932
UN(2,2)	ID	3.2694	1.2970

Solutions for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	-6.4800	1.1756	292	-5.51	<.0001
Treatment	-0.1972	1.2264	1325	-0.16	0.8723
Month	-1.4157	0.3634	287	-3.90	0.0001
Treatment*Month	-0.1545	0.1913	1325	-0.81	0.4194

Q=10 and T= 7.4 sec

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
UN(1,1)	ID	93.1842	19.6569
UN(2,1)	ID	-6.1591	1.6685
UN(2,2)	ID	1.0910	0.2606

Solutions for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	-3.5233	1.0978	292	-3.21	0.0015
Treatment	-0.2423	1.4467	1325	-0.17	0.8670
Month	-0.9130	0.2175	287	-4.20	<.0001
Treatment*Month	-0.2169	0.2012	1325	-1.08	0.2811

Q=20 and T= 36 sec

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
UN(1,1)	ID	179.91	51.2581
UN(2,1)	ID	-13.4084	4.3381
UN(2,2)	ID	2.1557	0.6290

Solutions for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	-5.3596	1.5727	292	-3.41	0.0007
Treatment	-0.2160	1.6621	1325	-0.13	0.8966
Month	-0.8947	0.2171	287	-4.12	<.0001
Treatment*Month	-0.5754	0.2400	1325	-2.40	0.0167

Q=50 and T= 3 minutes and 08 seconds

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
UN(1,1)	ID	76.1561	20.9446
UN(2,1)	ID	-5.5172	1.8133
UN(2,2)	ID	1.1002	0.3236

Solutions for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	-2.6926	0.9627	292	-2.80	0.0055
Treatment	-0.07782	1.2446	1325	-0.06	0.9502
Month	-0.8318	0.1827	287	-4.55	<.0001
Treatment*Month	-0.3521	0.1873	1325	-1.88	0.0603

GEE vs GLMM

Now let's fit the same model using GEE.

```
proc gee data=toenail descend;
class id;
model Response=Treatment Month Treatment*Month /d=bin link=logit;
repeated subject=ID/corr=UN corrw;
run;
```

Let's look at the results:

Analysis Of GEE Parameter Estimates

Empirical Standard Error Estimates

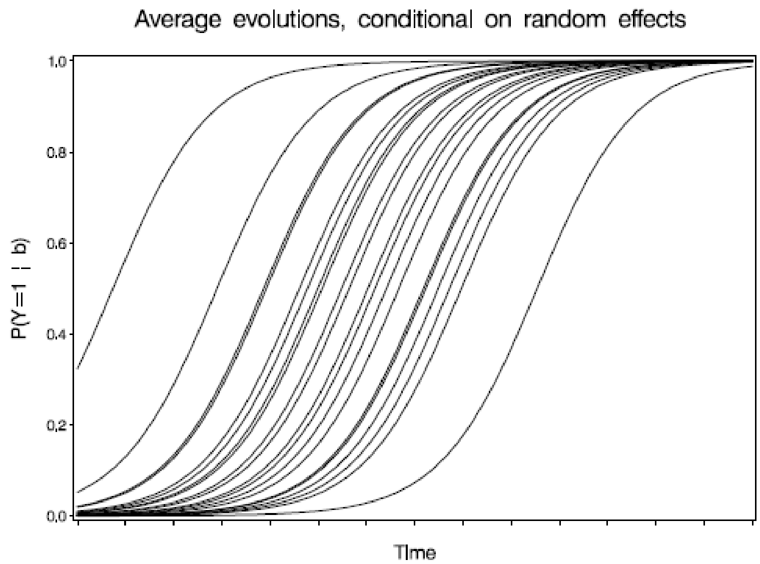
Parameter	Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept	-0.7625	0.1695	-1.0947	-0.4304	-4.50	<.0001
Treatment	0.0451	0.2550	-0.4548	0.5449	0.18	0.8597
Month	-0.1277	0.0260	-0.1786	-0.0768	-4.92	<.0001
Treatment*Month	-0.0866	0.0480	-0.1807	0.0075	-1.80	0.0713

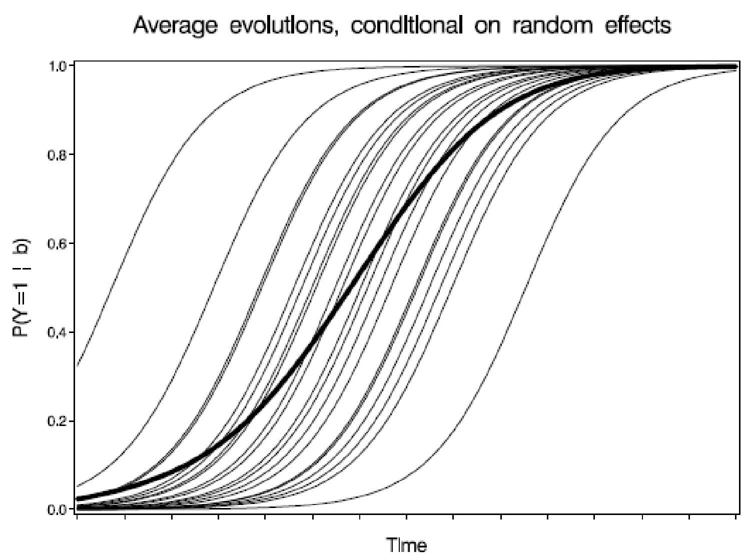
For the GLMM with Q=50 we had

Solutions for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	-2.6926	0.9627	292	-2.80	0.0055
Treatment	-0.07782	1.2446	1325	-0.06	0.9502
Month	-0.8318	0.1827	287	-4.55	<.0001
Treatment*Month	-0.3521	0.1873	1325	-1.88	0.0603

How to explain the differences





The parameter vector in the GEE model needs to be interpreted completely different from the parameter vector in the GLMM:

- GEE: marginal interpretation
- GLMM: conditional interpretation, conditionally upon level of random effects

In general, the model for the marginal average is not of the same parametric form as the conditional average in the GLMM.

The coefficients for a logistic mixed model with normally distributed random intercepts, can be approximated by again a logistic GEE model

$$\frac{\beta_{GLMM}}{\beta_{GEE}} = \sqrt{c^2\sigma^2 + 1} > 1$$

Where σ is the standard deviation of the random intercepts and c = 0.5881. In the toenail example we had random intercepts and slopes.

If we change to random intercepts only we get:

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
UN(1,1)	**ID**	16.0531	3.0441

Solutions for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	-1.6183	0.4343	292	-3.73	0.0002
Treatment	-0.1609	0.5840	1612	-0.28	0.7830
Month	-0.3910	0.04438	1612	-8.81	<.0001
Treatment*Month	-0.1368	0.06801	1612	-2.01	0.0444

For the Toenail example σ was 4.001 with makes $\sqrt{c^2\sigma^2 + 1} = 2.559$. Using this we get

Effect	GLMM Estimate	GLMM/2.559	GEE
Intercept	-1.6183	-0.632	-0.7625
Treatment	-0.1609	-0.063	0.0451
Month	-0.3910	-0.153	-0.1277
Treatment*Month	-0.1368	-0.053	-0.0866

In general the coefficients from GLMM are larger in absolute value than those from GEE.