Results

- The table below (Table __) shows the estimate, standard error, test statistic, and p-values associated with the fixed-effect slope parameter as estimated by each modeling method.

Model Designation	Model Description	Variable Pairing	Estimate	Std. Error	Test Statistic	p-value
LM	Linear Model	MALAT1-CD19	4.918e-2	1.455e-2	3.381	7.47e-4
		FBLN1-CD34	7.884e-1	4.92e-2	4.002	<2e-16
LM-FE	Linear Model Fixed Effect Intercept	MALAT1-CD19	4.833e-2	1.381e-2	3.500	4.84e-4
		FBLN1-CD34	1.31e-1	3.42e-2	3.818	1.42e-4
LM-RI	Linear Model Random Intercept	MALAT1-CD19	4.920e-2	1.374e-2	3.579	3.6e-4
		FBLN1-CD34	1.35e-1	3.42e-2	3.95	8.4e-5
LM-RS	Linear Model Random Slope	MALAT1-CD19	5.938e-2	3.538e-2	1.678	1.19e-1
		FBLN1-CD34	1.705e-1	7.29e-2	2.34	6.7e-2
GEE	Generalized Estimating Equations	MALAT1-CD19	4.918e-2	1.455e-2	3.381*	7.47e-4
		FBLN1-CD34	7.884e-1	4.92e-2	4.002*	< 2e-16

Table : Summary table for each model method, and each variable pairing. ** Approximate Wald-Z distribution

- The fixed effect slope parameter is being considered for comparison because:
  - It has been estimated in all models, so the effects on the parameter itself can be interpreted as effects due to model-approach changes
  - It will allow us to diagnose effects due to subject-level clustering when we compare

properties of the parameter across different modeling techniques

- Displayed:
  - percent change in: parameter estimate, standard error, and test statistic for the MALAT1~CD19 variable pairing as defined by:

$$\text{Percent Change}[A]_{ij} = \left(\frac{A_j - A_i}{A_i}\right) * 100$$

Model	Measure	LM	LM-FE	LMM-RI	LMM-RS	GEE
	Estimate	0	-1.7283	0.0407	20.7401	0.0000
LM	SE	0	-5.0859	-5.5670	143.1615	0.0000
	Test-Stat	0	3.5197	5.8563	-50.3697	0.0000
	Estimate	1.7587	0	1.8001	22.8636	1.7587
LM-FE	SE	5.3584	0	-0.5069	156.1912	5.3584
	Test-Stat	-3.4000	0	2.2571	-52.0571	-3.4000
	Estimate	-0.0407	-1.7683	0	20.6911	-0.0407
LMM-RI	SE	5.8952	0.5095	0	157.4964	5.8952
	Test-Stat	-5.5323	-2.2073	0	-53.1154	-5.5323
	Estimate	-17.1775	-18.6090	-17.1438	0	-17.1775
LMM-RS	SE	-58.8751	-60.9666	-61.1645	0	-58.8751
	Test-Stat	101.4899	108.5816	113.2896	0	101.4899
	Estimate	0.0000	-1.7283	0.0407	20.7401	0
GEE	SE	0.0000	-5.0859	-5.5670	143.1615	0
	Test-Stat	0.0000	3.5197	5.8563	-50.3697	0

Table: percent change in parameter estimate, standard error, and test statistic for the MALAT1-CD19 variable

- Displayed:
  - percent change in: parameter estimate, standard error, and test statistic for the

FBLN1~CD34 variable pairing

Model	Measure	LM	LM-FE	LMM-RI	LMM-RS	GEE
	Estimate	0	-83.3841	-82.8767	-78.3739	0.0000
LM	SE	0	-30.4878	-30.4878	48.1707	0.0000
	Test-Stat	0	-4.5977	-1.2994	-41.5292	0.0000
	Estimate	501.8321	0	3.0534	30.1527	501.8321
LM-FE	SE	43.8596	0	0.0000	113.1579	43.8596
	Test-Stat	4.8193	0	3.4573	-38.7114	4.8193
	Estimate	484.0000	-2.9630	0	26.2963	484.0000
LMM-RI	SE	43.8596	0.0000	0	113.1579	43.8596
	Test-Stat	1.3165	-3.3418	0	-40.7595	1.3165
	Estimate	362.4047	-23.1672	-20.8211	0	362.4047
LMM-RS	SE	-32.5103	-53.0864	-53.0864	0	-32.5103
	Test-Stat	71.0256	63.1624	68.8034	0	71.0256
	Estimate	0.0000	-83.3841	-82.8767	-78.3739	0
GEE	SE	0.0000	-30.4878	-30.4878	48.1707	0
	Test-Stat	0.0000	-4.5977	-1.2994	-41.5292	0

Table: percent change in parameter estimate, standard error, and test statistic for the FBLN1-CD34 variable

- Camparison of parameter estimates
  - We compare changes in the parameter estimate values because:
    * magnitude of change when comparing two model estimates can be indicative of the amount of subject-level correlation in the data
  - Findings:
    * Models LM and GEE have similar estimates -indicates that models with population-average interpretation parameters are more similar to each other
    * Models LM-FE, LM-RI, and LM-RS are also all similar -indicates that models with subject-specific interpretation parameters are more similar to each other

    * Estimates are less similar when comparing between the two clusters of similarity mentionioned
    * Accounting for subject-specific outcomes, results in a different estimate than when modeling population-averages, i.e. there is an effect from subject-level correlation
    * The effect is more pronounced in the FBLN1~CD34 pairing than the MALAT1~CD19 pairing

Standard Error Estimates

- Comparison of standard error of estimates
  - We compare changes in the standard error of estimates because:
    * a change in a parameter's SE across modeling methodologies represents a revision in the underlying evidence the method is using to support its result.
    * e.g. increase SE between two models indicates a decrease in an estimate's precision
  - Findings:
    * The standard error of the fixed effect slope parameter estimate is highest for the random slope model, which differs from all models with the incorperation of subject-specific variablility relationships between predictor and response
    * The SE is lowest for the random intercept model, which differs from all models either by lacking the incorperation of subject-specific varibility relationships between predictor and response (i.e. nested within LMM-RS model), or incorperating subject-specific variability information independent of predictors
    * The fixed-effect subject-specific intercept had a lower SE than either of the population-average parameter interpretaion models LM and GEE. The LM-FE model incorperates subject-specific predictor-independent information into the mean-effect of the model.

Test Statistics

- Comparison of test statistics
  - we compare changes in the test-statistics of estimates because:
    * patterns we observe in test statistic percent change matrices can serve to reinforce previous conclusions we have made using estimated coefficients and standard errors.
  - Findings:
    * Changes in test statistics for the fixed-effect main-effect slope were smaller between LM and GEE, as well as between LM-FE, LMM-RI, and LMM-RS with few exceptions.
    * There was undetectable change between LM and GEE
    * Changes to the LMM-RS resulted in loss of significance (larger p-value)

Nested Model Comparisons

Test for FE Subject Specific Intercept

Variable Pair	Model	Resid DF	RSS	DF	Sum of Squares	F-stat	P(>F)
MALAT1-CD19	LM	1108	1167.76				
	LM-FE	1094	935.89	14	231.87	19.36	$< 2.2e-16$
FBLN1-CD34	LM	1108	650.51				
	LM-FE	1094	214.92	14	435.59	158.38	$< 2.2e-16$

Table #: ANOVA nested model comparison table for testing the inclusion of the subject-specific fixed-effect intercept

The table above is a nested model comparison, the result of which is an F-test statistic telling us that there is very strong evidence to support the inclusion of the subject-specific fixed-effect intercept into the LM model.

Test for RE Subject Specific Intercept

Variable Pair	Model	df	AIC	logLik	L.Ratio	p-value
MALAT1-CD19	LM	3	3224.097	-1609.048		
	LMM-RI	4	3032.024	-1512.012	194.0722	<0.0001
FBLN1-CD34	LM	3	2572.807	-1283.403		
	LMM-RI	4	1438.086	-715.043	1136.72	<0.0001

Table #: ANOVA nested model comparison table for testing the inclusion of the subject-specific random effect intercept

The table above is a nested model comparison, the result of which is a likelihood ratio statistic telling us that there is very strong evidence to support the inclusion of the subject-specific random effect intercept into the LM model.

Test for RE Subject Specific Slope

Variable Pair	Model	df	AIC	logLik	L.Ratio	p-value
MALAT1-CD19	LMM-RI	4	3032.024	-1512.012		
	LMM-RS	6	2993.820	-1490.910	42.20503	<0.0001
FBLN1-CD34	LMM-RI	4	1438.086	-715.043		
	LMM-RS	6	1438.068	-713.034	4.018095	0.1341

Table #: ANOVA nested model comparison table for testing the inclusion of the subject-specific random effect slope

The table above is a nested model comparison, the result of which is a likelihood ratio statistic telling us that there is very strong evidence to support the inclusion of the subject-specific random effect slope into the LMM-RI model for the MALAT1~CD19 variable pairing. However, there is insufficient evidence to support the inclusion of the subject-specific random effect slope into the LMM-RI model for the FBLN~CD34 variable pairing.

References