Table 1

Summary of methods for analyzing longitudinal study data

	Change score analysis	Repeated measures ANOVA	Multivariate ANOVA (MANOVA)	Generalized estimating equations (GEE)	Mixed effect regression (MER)[a]
Description	Analyzes differences between outcomes measured at two time points.	Uses two main factors and an interaction term to assess group differences over time	Repeated responses over time treated as multivariate observations.	Designed for analyzing the regression relationship between covariates and repeated responses. GEEs do not allow inference on correlation structure of the repeated responses, but MERs do.	
Number of time points	Only 2.	Multiple.	Multiple.	Multiple.	Multiple.
Irregularly timed data	No.	No.	No.	Yes.	Yes.
Time-varying predictors	Not allowed.	Time treated as classification variable.	Time treated as classification variable.	Allowed.	Allowed.
How correlation between repeated responses modeled	Not applicable.	Assumes outcomes have equal variances and covariances over time.	No specific assumption.	Working models[b] that may or may not resemble observed correlations.	Random effects that quantify variation among units and serve to describe cluster-specific trends over time.
Missing data	Requires complete data. Analysis based on complete-cases or imputed missing values.[c] 1. Method yields unbiased parameter estimates and standard errors for (a) complete-case analysis when missingness is MCAR, (b) multiple imputation when missingness is MCAR or MAR. 2. Method yields only unbiased parameter estimates for (a) single mean imputation when missingness is MCAR, (b) conditional mean imputation when missingness is MCAR or MAR.			Handles missing data without explicit imputation needed. GEEs assume missingness is MCAR. Mixed effects regression assume missingness is MAR.	

[a]Preferred FDA method for incomplete longitudinal data

[b]Working models are typically one of four choices: independent, exchangeable, autocorrelation, unstructured (“Modeling correlation” section). Even when the working model is incorrect, regression parameter estimates are consistent, but associated standard errors are not.

Agresti [17] has recommendations for correcting standard error estimates

[c]*MCAR* missing completely at random, *MAR* missing at random