

Table 1. Type I error rates for the ML linear mixed (standard and sandwich corrected) and the ULS (standard and sandwich corrected) procedures. We simulated a genetic marker having a MAF=.5 and no effect on the trait. The sample consisted of N=4000 individuals. The trait was simulated according to an AE background model (the true model) given various heritabilities (h^2) (1 000 000 simulated samples for each cell). The background model in the ML procedure is correctly specified (true or saturated, i.e., unstructured).

A. $h^2=70\%$

Family structure	alpha	ML standard true model	ULS standard	Sandwich corrected ULS	Sandwich corrected ML (unstructured)
2 parents & 4 sibs	.05	0.049	0.15	0.05	0.05
	.01	0.01	0.06	0.01	0.01
	.001	0.001	0.017	0.001	0.001
	.0001	0.00009	0.0048	0.0001	0.0001
4 sibs	.05	0.049	0.12	0.05	0.05
	.01	0.01	0.04	0.01	0.01
	.001	0.001	0.01	0.001	0.001
	.0001	0.0001	0.0024	0.0001	0.0001

B. $h^2=50\%$

Family structure	alpha	ML standard true model	ULS standard	Sandwich corrected ULS	Sandwich corrected ML (unstructured)
2 parents & 4 sibs	.05	0.05	0.12	0.05	0.05
	.01	0.01	0.044	0.01	0.01
	.001	0.001	0.01	0.001	0.001
	.0001	0.00009	0.0024	0.0001	0.0001
4 sibs	.05	0.05	0.1	0.05	0.05
	.01	0.01	0.03	0.01	0.01
	.001	0.001	0.006	0.001	0.001
	.0001	0.0001	0.001	0.0001	0.0001

C. $h^2=30\%$

Family structure	alpha	ML standard true model	ULS standard	Sandwich corrected ULS	Sandwich corrected ML (unstructured)
2 parents & 4 sibs	.05	0.05	0.096	0.05	0.05
	.01	0.01	0.029	0.01	0.01
	.001	0.001	0.005	0.001	0.001
	.0001	0.0001	0.001	0.0001	0.0001
4 sibs	.05	0.05	0.08	0.05	0.05
	.01	0.01	0.02	0.01	0.01
	.001	0.001	0.003	0.001	0.001
	.0001	0.0001	0.0005	0.0001	0.0001

Table 2. Type I error rates for the ML linear mixed (standard and sandwich corrected) and the ULS (standard and sandwich-corrected) procedures. The background model is a) correctly specified (true) or b) misspecified. Background covariance matrix was generated according to an ACE model ($h^2=.6$, $c^2=.2$). The samples comprised of 4000 individuals (1 000 000 simulated data sets/cell).

Family structure	alpha	ML standard ACE model (true)	ML standard AE model (false)	ML standard CE model (false)	Sandwich corrected ML (false: AE structured)	Sandwich corrected ML (false: CE structured)	ULS standard E model (false)	Sandwich corrected ULS E model (false)
2 parents & 4 sibs	0.05	0.05	0.050	0.07	0.05	0.05	0.19	0.05
	0.01	0.0099	0.0099	0.019	0.01	0.01	0.08	0.01
	0.001	0.001	0.0009	0.0027	0.001	0.001	0.028	0.001
	0.0001	0.00008	0.00009	0.0004	0.00009	0.00011	0.009	0.00011
4 sibs	0.05	0.05	0.049	0.06	0.05	0.05	0.15	0.05
	0.01	0.01	0.0099	0.014	0.01	0.01	0.06	0.01
	0.001	0.001	0.001	0.0018	0.001	0.001	0.01	0.001
	0.0001	0.0001	0.00009	0.0002	0.0001	0.0001	0.004	0.00008

Table 3. Power (given $\alpha=10^{-7}$) and parameter estimates for the ML (standard and sandwich corrected) and the ULS (standard and sandwich corrected) procedures. The background model is a) correctly specified (true) or b) misspecified. Background covariance matrix was generated according to an ACE model ($h^2=.6$, $c^2=.2$). The genetic marker explained 1% phenotypic variance and had a MAF=.5. The samples consisted of N=4000 individuals (10 000 simulated data sets per cell).

Family structure		ML standard ACE model (true)	ML standard AE model (false)	ML standard CE model (false)	Sandwich corrected ML (false: AE structured)	Sandwich corrected ML (false: CE structured)	ULS standard E model (false)	Sandwich corrected ULS E model (false)
2 parents & 4 sibs	mean (b_1)	-0.142	-0.142	-0.142	-0.142	-0.142	-0.142	-0.142
	mean (st.err.)	0.024	0.024	0.022	0.024	0.024	0.022	0.033
	mean (t-value)	-6.02	-5.95	-6.39	-5.95	-5.82	-6.36	-4.24
	power	75.6	73.4	83.8	73.1	68.8	75.7	14.3
4 sibs	mean (b_1)	-0.142	-0.142	-0.142	-0.142	-0.142	-0.142	-0.142
	mean (st.err.)	0.023	0.024	0.022	0.024	0.024	0.022	0.031
	mean (t-value)	-6.03	-5.97	-6.30	-5.98	-5.98	-6.37	-4.65
	power	75.7	73.8	81.8	74.1	74.2	77.5	25.1

Table 4. Power and parameter estimates for the ML and the ULS (standard and sandwich corrected) procedures. The background model is a) correctly specified (true) or b) misspecified. Background covariance matrix was generated according to an ADE model ($h^2=.5$, $d^2=.2$). The genetic marker explained .5% phenotypic variance and had a MAF=.5. The samples consisted of 500 MZ and 500 DZ size 4 sibships (twins and 2 sibs). We used 10 000 replications per cell.

alpha		ML standard ADE model (true)	ML standard AE model (false:)	Sandwich corrected ML (false: AE structured)	ULS standard E model (false)	Sandwich corrected ULS E model (false)
0.05	mean (b_1)	-0.099	-0.099	-0.099	-0.099	-0.099
	mean (st.err.)	(0.025)	(0.025)	(0.025)	(0.022)	(0.028)
	power	99.1	99.1	99.1	98.8	97.2
0.01	mean (b_1)	-0.099	-0.099	-0.099	-0.099	-0.099
	mean (st.err.)	(0.025)	(0.025)	(0.025)	(0.022)	(0.028)
	power	94.9	94.9	95.0	95.9	89.0
0.001	mean (b_1)	-0.099	-0.099	-0.099	-0.099	-0.099
	mean (st.err.)	(0.025)	(0.025)	(0.025)	(0.022)	(0.028)
	power	81.4	81.3	81.1	86.4	67.4
1e-04	mean (b_1)	-0.099	-0.099	-0.099	-0.099	-0.099
	mean (st.err.)	(0.025)	(0.025)	(0.025)	(0.022)	(0.028)
	power	60.1	59.8	59.8	72.4	43.6
1e-05	mean (b_1)	-0.099	-0.099	-0.099	-0.099	-0.099
	mean (st.err.)	(0.025)	(0.025)	(0.025)	(0.022)	(0.028)
	power	38.5	38.1	38.5	56.6	23.8
1e-06	mean (b_1)	-0.099	-0.099	-0.099	-0.099	-0.099
	mean (st.err.)	(0.025)	(0.025)	(0.025)	(0.022)	(0.028)
	power	22.3	22.0	22.2	41.0	12.1

1e-07	mean (b ₁)	-0.099	-0.099	-0.099	-0.099	-0.099
	mean (st.err.)	(0.025)	(0.025)	(0.025)	(0.022)	(0.028)
	power	11.2	11.0	11.3	27.9	5.2

Table 5. Type I error rates for the ML linear mixed (standard), the Generalized Estimating Equations (GEE) (standard and sandwich corrected) and the ULS (standard and sandwich corrected) procedures. Type I error rates were assessed for the continuous trait and following dichotomization of the continuous trait (by median split). We simulated a genetic marker having a MAF=.5 and no effect on the trait. The sample consisted of N=4000 individuals. The continuous trait was simulated according to an AE background model (the true model), where additive genetic factors explained 70% of the phenotypic variance. The background model is a) correctly specified (true) or b) misspecified (100 000 simulated samples for each cell).

	ML standard true model	GEE standard (false: CE structured)	Sandwich corrected GEE (false: CE structured)	ULS standard E model (false)	Sandwich corrected ULS E model (false)	GEE standard (false: CE structured)	Sandwich corrected GEE (false: CE structured)	GEE standard E model (false)	Sandwich corrected GEE E model (false)
phenotype	continuous					dichotomized (median split)			
alpha=.05	0.051	0.061	0.051	0.128	0.050	0.057	0.051	0.101	0.050
alpha=.01	0.010	0.014	0.011	0.045	0.010	0.012	0.010	0.032	0.010
alpha=.001	0.001	0.002	0.001	0.011	0.001	0.001	0.001	0.006	0.001

Table 6. Power (given $\alpha=10^{-7}$) and parameter estimates for the ML linear mixed (standard), the Generalized Estimating Equations (GEE) (standard and sandwich corrected) and the ULS (standard and sandwich corrected) procedures. Power was assessed for the continuous trait and following dichotomization of the continuous trait (by median split). The background model is a) correctly specified (true) or b) misspecified. Background covariance matrix was generated according to an AE model ($h^2=.7$). The genetic marker explained 1% phenotypic variance and had a MAF=.5. The samples consisted of N=4000 individuals (10 000 data sets per cell).

	ML standard true model	GEE standard (false: CE structured)	Sandwich corrected GEE (false: CE structured)	ULS standard E model (false)	Sandwich corrected ULS E model (false)	GEE standard (false: CE structured)	Sandwich corrected GEE (false: CE structured)	GEE standard E model (false)	Sandwich corrected GEE E model (false)	
phenotype	continuous					dichotomized (median split)				
mean (b1)	-0.141	-0.141	-0.141	-0.141	-0.141	-0.22	-0.22	-0.22	-0.22	
st.err.	0.025	0.024	0.025	0.022	0.029	0.049	0.051	0.045	0.054	
t-test	-5.7	-5.90	-5.66	-6.34	-4.94	-4.60	-4.50	-5.03	-4.21	
power	65.0	71.0	63.2	78.7	35.0	23.9	20.3	40.7	12.7	