Supplementary Materials for "A hybrid model for combining case-control and cohort studies in systematic reviews of diagnostic tests "

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Abstract

This Supplementary Material includes the derivation of the variance formula for the maximum composite likelihood estimator, calculation of the parameter d_s^* in the model selection criterion, more details on the motivating dataset, additional simulation results, and R and SAS codes with an illustrated example.

Section 1: Derivation of the variance formula for the maximum composite likelihood estimator

Denote $\boldsymbol{\theta} = (\boldsymbol{\theta_0}, \boldsymbol{\theta_1}, \boldsymbol{\theta_2})^T$. By Taylor expansion of $\partial \log L_c(\tilde{\boldsymbol{\theta}})/\partial \boldsymbol{\theta}$ around $\boldsymbol{\theta}$, we have

$$0 = \frac{1}{\sqrt{m}} \frac{\partial \log L_c(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}} + \frac{1}{m} \frac{\partial^2 \log L_c(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}^2} \sqrt{m}(\tilde{\boldsymbol{\theta}} - \boldsymbol{\theta}) + o_p(1). \tag{1}$$

Therefore, we have

$$\sqrt{m}(\tilde{\boldsymbol{\theta}} - \boldsymbol{\theta}) \approx {\mathbf{A_m}}^{-1} \frac{1}{\sqrt{m}} \mathbf{B_m}, \quad \text{where} \quad \mathbf{A_m} = -\frac{1}{m} \frac{\partial^2 \log L_c(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}^2} \quad \text{and} \quad \mathbf{B_m} = \frac{\partial \log L_c(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}.$$

It is easy to show that $\frac{1}{\sqrt{m}} \mathbf{B_m} \to N(0, {\boldsymbol{\Sigma_1}}^*)$ where

$${\boldsymbol{\Sigma_1}}^* = \begin{pmatrix} r\mathbf{I_{00}} & \sqrt{r}\mathbf{I_{01}} & \sqrt{r}\mathbf{I_{02}} \\ & \mathbf{I_{11}} & \mathbf{I_{12}} \\ & & \mathbf{I_{22}} \end{pmatrix} \quad \text{and} \quad \mathbf{A_m} \to {\boldsymbol{\Sigma_2}}^* = \begin{pmatrix} r\mathbf{I_{00}} & 0 & 0 \\ & \mathbf{I_{11}} & 0 \\ & & \mathbf{I_{22}} \end{pmatrix},$$

where $m_2/m \to r$. The asymptotic distribution is immediately followed by Slutsky's theorem and recalling equation (1).

Section 2: Calculation of d_s^*

When the meta-analysis model does not include study-level covariates, the composite likelihood contains 6 parameters: $(\beta_0, \beta_1, \beta_2, \tau_0^2, \tau_1^2, \tau_2^2)$. We first show that d_s^* converges to 6. By definition $d_s^* = \text{trace}\left\{\hat{J}(\hat{H})^{-1}\right\}$, where $\hat{J}$ and $\hat{H}$ converge to ${\boldsymbol{\Sigma_1}}^*$ and ${\boldsymbol{\Sigma_2}}^*$, respectively. By the calculation of ${\boldsymbol{\Sigma_1}}^*$ and ${\boldsymbol{\Sigma_2}}^*$ in Section 1, we have $d_s^* = \text{trace}\left\{\hat{J}(\hat{H})^{-1}\right\}$ converges to 6 as the number of studies m increases. This result is due to the information identity holds for each component of the composite likelihood function $\log L_c(\boldsymbol{\theta_0}, \boldsymbol{\theta_1}, \boldsymbol{\theta_2})$. Similar argument can be applied to show the results for meta-analysis model with study-level covariates.

Section 3: Cross-tabulate of case-control and cohort studies by subtype of cancer

Table S1: Numbers of case-control and cohort studies collected by Xing et al., (2011) stratified by the type of metastasis (i.e., regional versus distant metastasis) and the type of imaging modalities

Types	**Case-Control** (# of study)	**Cohort** (# of study)
Regional metastasis		
Ultrasonography (US)	6	14
Computed Tomography (CT)	2	1
Positron Emission Tomography (PET)	5	16
Combination of both (PET-CT)	3	2
Distant metastasis		
Computed Tomography (CT)	7	5
Positron Emission Tomography (PET)	14	15
Combination of both (PET-CT)	4	4

Section 4: Impact of initial values on the estimates using the full likelihood and the composite likelihood methods

Table S2: Impact of initial values on the estimates using the full likelihood (FL) and the composite likelihood (CL) methods when analyzing the distant metastasis data in Xing et al. (2011).

Imaging modality	**Initial value** $(\beta_0, \beta_1, \beta_2, \tau_0, \tau_1, \tau_2, \rho_{01}, \rho_{02}, \rho_{12})$	**FL method** $(\hat{\beta}_0, \hat{\beta}_1, \hat{\beta}_2)$	**CL method** $(\hat{\beta}_0, \hat{\beta}_1, \hat{\beta}_2)$
PET-CT	(0, 0, 0, 1, 1, 1, 0, 0, 0)	non-convergent	(0.24, 1.75, 2.68)
$(m_1 = m_2 = 4)$	(1, 1, 1, 1, 1, 1, 0.1, -0.1, -0.1)	non-convergent	(0.24, 1.75, 2.68)
CT	(0, 0, 0, 1, 1, 1, 0, 0, 0)	non-convergent	(-0.16, 0.58, 1.87)
$(m_1 = 7, m_2 = 5)$	(2.1, 1, 1, 1, 1, 1, 0, 0, 0)	non-convergent	(-0.16, 0.58, 1.87)
	(2.1, 1.2, 1, 1, 1, 1, 0, 0, 0)	(0.15, 0.60, 1.86)	(-0.16, 0.58, 1.87)
PET	(0, 0, 0, 1, 1, 1, 0, 0, 0)	(0.37, 1.69, 1.94)	(0.36, 1.71, 1.94)
$(m_1 = 14, m_2 = 15)$	(1, 1, 1, 1, 1, 1, -0.1, -0.1, -0.1)	(0.37, 1.69, 1.94)	(0.36, 1.71, 1.94)
	(3, 2.8, 4, 2, 2, 2, 0.2, 0.3, 0.1)	(0.47, 1.65, 1.97)*	(0.36, 1.71, 1.94)

m_1: number of case-control studies; m_2: number of cohort studies.
*: singular covariance matrix.

Section 5: Additional simulation results

Tables S3 $\sim$ S8 summarize the simulations with that data are generated from the bivariate GLMM (for case-control studies) and trivariate GLMM (for cohort studies) model when the number of studies are 8, 30 and 50. When the number of studies is 8, the biases of the estimates from both FL and CL methods are small but they underestimate the true standard errors, leading to liberal confidence intervals. We note that when the number of studies is relatively small (e.g., $m = 8$), resampling methods such as bootstrap are recommended to obtain better estimates of standard errors. Tables S9 $\sim$ S10 summarize the results when study-level covariates are available and the number of studies are 30 and 50, respectively. Both method provide unbiased estimates, but the CL method has better coverages compared to the FL method. Tables

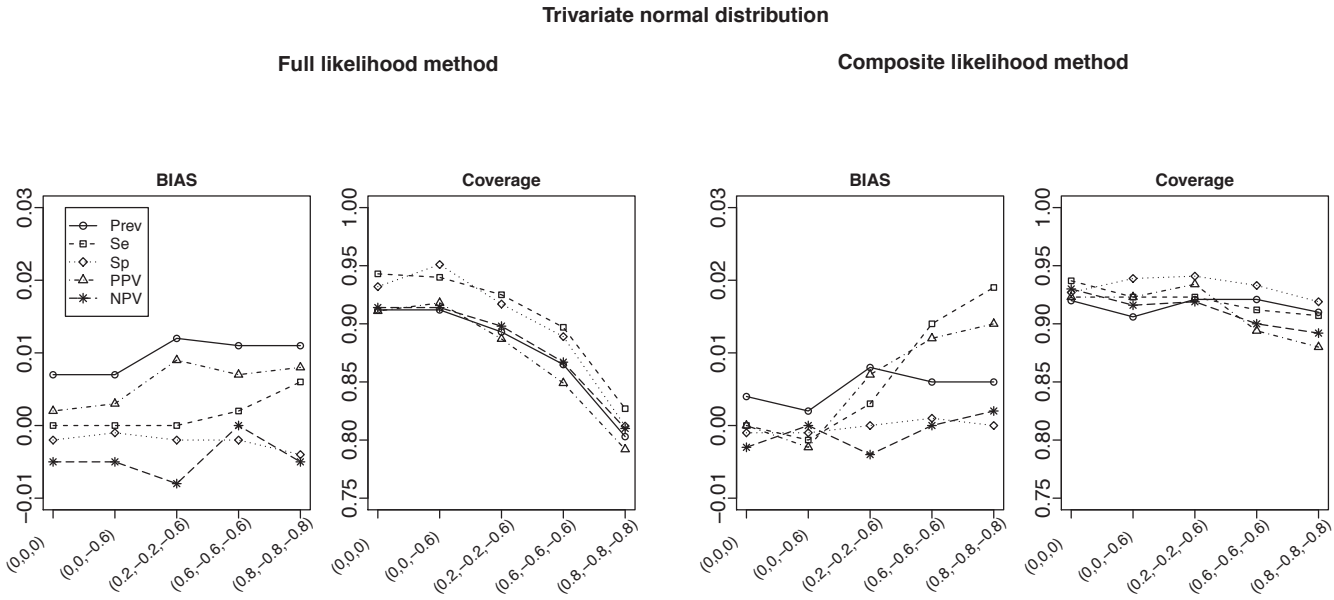

Figure S1: Bias and coverage for estimated disease prevalence, sensitivity, specificity, PPV and NPV from the full likelihood (FL) and the composite likelihood (CL) methods. The true overall disease prevalence is 0.2, sensitivity is 0.6, and specificity is 0.9. The data are generated from bivariate GLMM (for case-control studies) and trivariate GLMM (for cohort studies). Results are summarized from 1000 simulations. The x-axis represents for the different settings of pairwise correlations among study-specific prevalence, sensitivity and specificity (in logit scale).

S11 $\sim$ S16 summarize the results when study-specific prevalence, sensitivity and specificity form the bivariate *t-distribution* (for case-control studies) and the trivariate *t-distribution* (for cohort studies) with 4 degrees of freedom with m= 8, 30 and 50 studies.

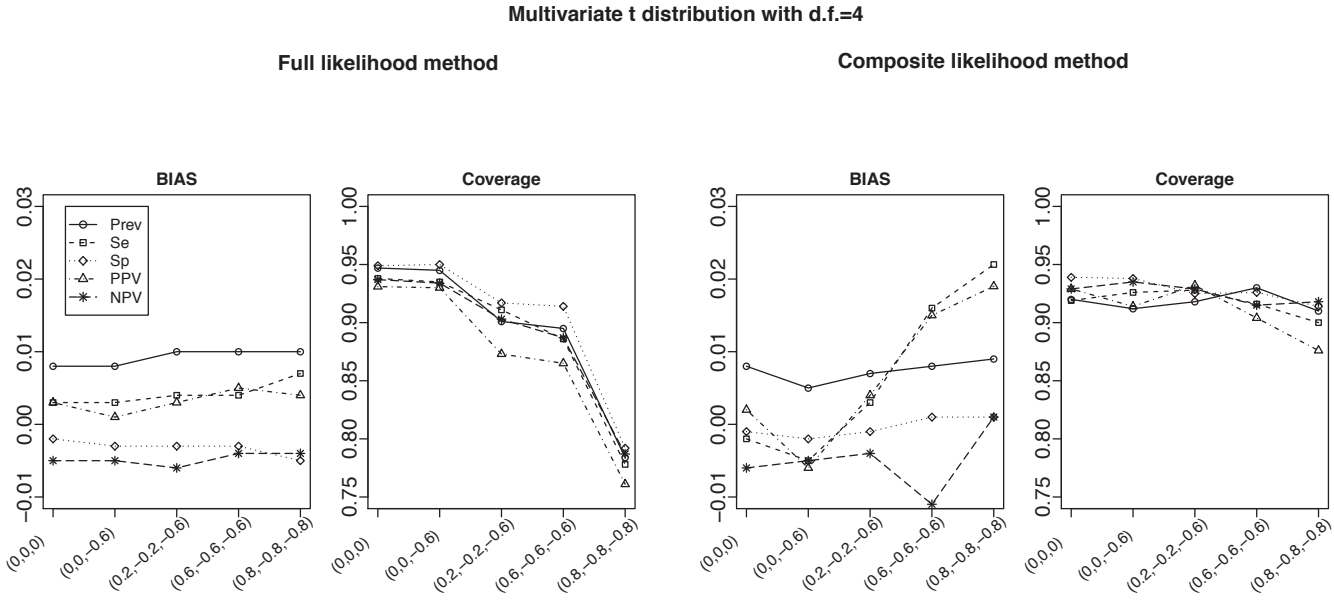

Figure S2: Bias and coverage for estimated disease prevalence, sensitivity, specificity, PPV and NPV from the full likelihood (FL) and the composite likelihood (CL) methods. The true overall disease prevalence is 0.2, sensitivity is 0.6, and specificity is 0.9. The data are generated from bivariate *t-distribution* (for case-control studies) and trivariate *t-distribution* (for cohort studies). Results are summarized from 1000 simulations. The x-axis represents for the different settings of pairwise correlations among study-specific prevalence, sensitivity and specificity (in logit scale).

Table S3: Summary of 1,000 simulations with 8 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall disease prevalence and diagnostic test sensitivity and specificity.

		BIAS	SE	MBSE	CP	RE	MEAN	SE	MBSE	CP	RE	MEAN	SE	MBSE	CP	RE
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Sensitivity = .600					Specificity = .900				
(.0, .0, .0)	FL	.024	.089	.070	.795	1.000	-.008	.098	.089	.869	1.000	-.006	.041	.034	.856	1.000
	CL	.019	.085	.071	.834	1.096	-.004	.108	.091	.828	.823	-.008	.039	.035	.881	1.105
(.0, .0, -.6)	FL$^{\pm}$	.020	.090	.092	.886	1.000	-.009	.100	.168	.857	1.000	-.002	.040	.040	.822	1.000
	CL	.015	.086	.069	.812	1.095	-.002	.108	.092	.824	.857	-.007	.039	.035	.869	1.052
(.2, -.2, -.6)	FL†	.033	.104	.172	.453	1.000	.002	.101	.128	.457	1.000	-.004	.040	.070	.483	1.000
	CL	.025	.085	.071	.811	1.497	.004	.104	.092	.833	.943	-.005	.039	.034	.863	1.052
(.6, -.6, -.6)	FL‡	.023	.087	.091	.395	1.000	.007	.103	.107	.375	1.000	-.007	.040	.052	.415	1.000
	CL	.011	.082	.069	.802	1.126	.006	.104	.092	.852	.981	-.003	.040	.034	.850	1.000
(.8, -.8, -.8)	FL§	.032	.084	.128	.332	1.000	.019	.098	.209	.328	1.000	-.013	.044	.069	.314	1.000
	CL	.019	.086	.071	.816	.954	.022	.100	.089	.819	.960	-.005	.037	.034	.877	1.414
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Sensitivity = .900					Specificity = .900				
(.0, .0, .0)	FL	.024	.089	.070	.792	1.000	-.009	.048	.040	.861	1.006	-.006	.041	.034	.853	1.000
	CL	.017	.089	.069	.769	1.000	-.010	.050	.043	.838	.922	-.016	.039	.035	.875	1.105
(.0, .0, -.6)	FL$^{\wedge}$	.019	.089	.092	.877	1.000	-.006	.048	1.638	.796	1.000	-.002	.041	2.350	.777	1.000
	CL	.014	.088	.070	.796	1.023	-.009	.051	.042	.837	.886	-.008	.040	.036	.882	1.051
(.2, -.2, -.6)	FL*	.020	.102	.124	.350	1.000	-.004	.043	.097	.338	1.000	.000	.042	.070	.333	1.000
	CL	.019	.086	.069	.800	1.407	-.008	.050	.042	.845	.740	-.005	.039	.034	.867	1.160
(.6, -.6, -.6)	FL$^{\mp}$	.015	.082	.110	.364	1.000	.002	.048	.088	.374	1.000	-.008	.038	.073	.336	1.000
	CL	.012	.081	.068	.820	1.025	-.001	.047	.041	.839	1.043	-.003	.037	.034	.877	1.055
(.8, -.8, -.8)	FL*	.049	.104	.104	.364	1.000	-.097	.068	.085	.322	1.000	-.004	.040	.051	.368	1.000
	CL	.016	.087	.068	.775	1.429	.001	.046	.040	.817	2.186	-.003	.039	.034	.862	1.052

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method;
$^{\pm}$: the non-convergence rate was 13.4%; †: the non-convergence rate was 76.8%;
‡: the non-convergence rate was 75.2%; §: the non-convergence rate was 77.1%;
$^{\wedge}$: the non-convergence rate was 19.8%; *: the non-convergence rate was 76.3%;
$^{\mp}$: the non-convergence rate was 78.6%; *: the non-convergence rate was 75.8%.

Table S4: Summary of 1,000 simulations with 8 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall PPV and NPV. True values of PPV and NPV are (.600, .900) or (.692, .973).

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
$(\rho_{01}, \rho_{02}, \rho_{12})$		PPV = .600					NPV = .900				
(.0, .0, .0)	FL	.004	.148	.129	.829	1.000	-.019	.062	.050	.858	1.000
	CL	-.007	.146	.132	.884	1.028	-.014	.057	.052	.887	1.183
(.0, .0, -.6)	FL$^{\pm}$	.006	.144	.148	.834	1.000	-.016	.061	.074	.872	1.000
	CL	-.009	.143	.127	.889	1.014	-.012	.058	.050	.877	1.106
(.2, -.2, -.6)	FL†	.020	.143	.274	.431	1.000	-.022	.070	.102	.478	1.000
	CL	.013	.135	.118	.881	1.122	-.015	.055	.049	.861	1.620
(.6, -.6, -.6)	FL‡	.006	.139	.127	.403	1.000	-.011	.050	.057	.395	1.000
	CL	.000	.127	.112	.858	1.198	-.005	.047	.041	.860	1.132
(.8, -.8, -.8)	FL§	.017	.110	.154	.319	1.000	-.013	.043	.053	.410	1.000
	CL	.012	.121	.101	.857	.826	-.005	.047	.038	.842	.837
$(\rho_{01}, \rho_{02}, \rho_{12})$		PPV= .692					NPV = .973				
(.0, .0, .0)	FL	.000	.130	.111	.832	1.000	- .009	.025	.020	.887	1.000
	CL	-.011	.135	.117	.857	.927	-.007	.025	.021	.894	1.000
(.0, .0 -.6)	FL$^{\wedge}$	.002	.133	3.700	.804	1.000	-.006	.024	.718	.832	1.000
	CL	-.016	.130	.116	.893	1.047	-.006	.024	.020	.895	1.000
(.2, -.2, -.6)	FL*	.002	.137	.195	.329	1.000	-.006	.027	.038	.401	1.000
	CL	-.006	.128	.106	.855	1.146	-.006	.021	.019	.890	1.653
(.6, -.6, -.6)	FL$^{\mp}$	-.010	.113	.220	.393	1.000	-.003	.019	.029	.397	1.000
	CL	-.003	.112	.094	.853	1.018	-.002	.017	.016	.876	1.249
(.8, -.8, -.8)	FL*	.010	.116	.124	.355	1.000	-.042	.042	.039	.293	1.000
	CL	.004	.102	.082	.853	1.293	-.002	.016	.014	.882	6.891

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method;
$^{\pm}$: the non-convergence rate was 13.4%; †: the non-convergence rate was 76.8%;
‡: the non-convergence rate was 75.2%; §: the non-convergence rate was 77.1%;
$^{\wedge}$: the non-convergence rate was 19.8%; *: the non-convergence rate was 76.3%;
$^{\mp}$: the non-convergence rate was 78.6%; *: the non-convergence rate was 75.8%.

Table S5: Summary of 1,000 simulations with 30 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall disease prevalence and diagnostic test sensitivity and specificity.

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Diagnostic sensitivity = .600					Diagnostic specificity = .900				
(.0, .0, .0)	FL	.007	.045	.041	.912	1.000	.000	.047	.047	.943	1.000	-.002	.018	.018	.932	1.000
	CL	.004	.043	.041	.920	1.095	.000	.047	.047	.937	1.000	-.001	.019	.018	.927	.898
(.0, .0, -.6)	FL	.007	.045	.041	.912	1.000	.000	.047	.047	.940	1.000	-.001	.018	.018	.951	1.000
	CL	.002	.044	.041	.906	1.046	-.002	.049	.047	.923	.920	-.001	.019	.018	.939	.898
(.2, -.2, -.6)	FL†	.012	.048	.043	.893	1.000	.000	.053	.050	.925	1.000	-.002	.020	.019	.917	1.000
	CL	.008	.044	.042	.921	1.190	.003	.054	.054	.923	.963	.000	.019	.019	.941	1.108
(.6, -.6, -.6)	FL‡	.011	.046	.040	.865	1.000	.002	.050	.049	.897	1.000	-.002	.020	.019	.889	1.000
	CL	.006	.044	.042	.921	1.093	.014	.052	.052	.912	.925	.001	.019	.019	.933	1.108
(.8, -.8, -.8)	FL§	.011	.041	.039	.803	1.000	.006	.050	.049	.827	1.000	-.004	.020	.019	.812	1.000
	CL	.006	.045	.042	.910	.830	.019	.053	.052	.907	.890	.000	.019	.019	.919	1.108
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Diagnostic sensitivity = .900					Diagnostic specificity = .900				
(.0, .0, .0)	FL	.007	.045	.041	.912	1.000	-.002	.021	.020	.937	1.000	-.002	.018	.018	.932	1.000
	CL	.005	.044	.041	.915	1.046	-.001	.021	.020	.930	1.000	-.001	.019	.018	.920	.898
(.0, .0, -.6)	FL	.007	.045	.041	.908	1.000	-.002	.021	.020	.932	1.000	-.001	.018	.018	.945	1.000
	CL	.002	.043	.041	.924	1.095	-.001	.021	.020	.940	1.000	-.002	.018	.018	.942	1.000
(.2, -.2, -.6)	FL*	.012	.047	.043	.856	1.000	-.002	.023	.022	.892	1.000	-.002	.020	.019	.882	1.000
	CL	.009	.046	.043	.911	1.044	.001	.024	.023	.918	.918	-.001	.020	.019	.941	1.000
(.6, -.6, -.6)	FL$^{\mp}$	.010	.044	.040	.833	1.000	-.001	.022	.022	.849	1.000	-.002	.019	.019	.849	1.000
	CL	.007	.044	.042	.917	1.000	.006	.024	.022	.904	.840	-.001	.020	.019	.923	.903
(.8, -.8, -.8)	FL*	.009	.043	.040	.771	1.000	.001	.022	.021	.782	1.000	-.004	.021	.019	.773	1.000
	CL	.007	.044	.042	.920	.955	.007	.023	.022	.877	.915	.000	.019	.018	.922	1.222
heterogeneous $^{\diamond}$	FL$^{\pm}$	.014	.062	.041	.660	1.000	-.003	.033	.023	.691	1.000	-.004	.028	.022	.698	1.000
	CL	.008	.043	.041	.922	1.957	.001	.024	.023	.913	1.891	-.001	.020	.019	.922	1.960

$^{\diamond}$: half of the cohort studies have correlation structure of (.0, .0, -.6), and the remaining half are (.6, -.6, -.6).

†: the non-convergence rate was 10.9%; ‡: the non-convergence rate was 16.4%; §: the non-convergence rate was 34.1%;

*: the non-convergence rate was 22.8%; $^{\mp}$: the non-convergence rate was 28.0%; *: the non-convergence rate was 47.6%;

$^{\pm}$: the non-convergence rate was 42.0%.

Table S6: Summary of 1,000 simulations with 30 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall PPV and NPV. True values of PPV and NPV are (.600, .900) or (.692, .973).

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
$(\rho_{01}, \rho_{02}, \rho_{12})$		PPV = .600					NPV = .900				
(.0, .0, .0)	FL	.002	.078	.076	.911	1.000	-.005	.029	.026	.914	1.000
	CL	.000	.080	.076	.923	.951	-.003	.027	.026	.930	1.154
(.0, .0, -.6)	FL	.003	.073	.071	.918	1.000	-.005	.028	.026	.914	1.000
	CL	-.003	.076	.071	.923	.923	-.002	.027	.025	.916	1.075
(.2, -.2, -.6)	FL†	.009	.076	.071	.887	1.000	-.008	.029	.027	.898	1.000
	CL	.007	.072	.070	.934	1.114	-.004	.027	.025	.919	1.154
(.6, -.6, -.6)	FL‡	.007	.069	.062	.849	1.000	-.006	.025	.023	.867	1.000
	CL	.012	.067	.062	.894	1.061	.000	.024	.022	.900	1.085
(.8, -.8, -.8)	FL§	.008	.057	.055	.792	1.000	-.005	.021	.020	.810	1.000
	CL	.014	.063	.055	.880	.819	.002	.023	.020	.892	.834
$(\rho_{01}, \rho_{02}, \rho_{12})$		PPV= .692					NPV = .973				
(.0, .0, .0)	FL	.000	.067	.066	.921	1.000	-.002	.010	.009	.934	1.000
	CL	-.002	.069	.066	.920	.943	-.002	.010	.009	.920	1.000
(.0, .0, -.6)	FL	.002	.066	.065	.905	1.000	-.002	.010	.009	.925	1.000
	CL	-.006	.068	.065	.919	.942	-.001	.009	.009	.923	1.235
(.2, -.2, -.6)	FL*	.006	.066	.063	.855	1.000	-.003	.010	.009	.881	1.000
	CL	.006	.067	.061	.906	.970	-.001	.010	.009	.917	1.000
(.6, -.6, -.6)	FL$^{\mp}$	.005	.057	.053	.836	1.000	-.002	.009	.008	.850	1.000
	CL	.005	.057	.051	.895	1.000	.000	.009	.007	.897	1.000
(.8, -.8, -.8)	FL*	.002	.050	.050	.765	1.000	-.001	.007	.007	.763	1.000
	CL	.008	.053	.043	.853	.890	.001	.008	.007	.900	.766
heterogeneous $^{\diamond}$	FL$^{\pm}$	.007	.085	.065	.659	1.000	-.003	.013	.010	.702	1.000
	CL	.006	.063	.077	.945	1.820	-.001	.009	.009	.953	2.086

$^{\diamond}$: half of the cohort studies have correlation structure of (.0, .0, -.6), and the remaining half are (.6, -.6, -.6).
†: the non-convergence rate was 10.9%; ‡: the non-convergence rate was 16.4%;
§: the non-convergence rate was 34.1%; *: the non-convergence rate was 22.8%;
$^{\mp}$: the non-convergence rate was 28.0%; *: the non-convergence rate was 47.6%;
$^{\pm}$: the non-convergence rate was 42.0% .

Table S7: Summary of 1,000 simulations with 50 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall disease prevalence and diagnostic test sensitivity and specificity.

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Diagnostic sensitivity = .600					Diagnostic specificity = .900				
(.0, .0, .0)	FL	.004	.034	.033	.921	1.000	.000	.037	.036	.936	1.000	-.001	.014	.014	.945	1.000
	CL	.000	.033	.032	.917	1.062	-.001	.037	.037	.937	1.000	-.001	.014	.014	.927	1.000
(.0, .0, -.6)	FL	.004	.034	.033	.921	1.000	.000	.037	.036	.935	1.000	-.001	.014	.014	.941	1.000
	CL	.003	.034	.032	.934	1.000	-.001	.038	.037	.939	.948	-.002	.014	.014	.960	1.000
(.2, -.2, -.6)	FL	.007	.036	.034	.928	1.000	.000	.041	.039	.919	1.000	-.001	.016	.015	.928	1.000
	CL	.006	.034	.033	.933	1.121	.006	.044	.042	.924	.868	-.001	.016	.015	.928	1.000
(.6, -.6, -.6)	FL	.006	.033	.031	.925	1.000	.001	.040	.039	.921	1.000	-.001	.015	.015	.932	1.000
	CL	.007	.035	.034	.938	.889	.016	.042	.041	.914	.907	.000	.015	.015	.930	1.000
(.8, -.8, -.8)	FL†	.005	.031	.029	.910	1.000	.002	.039	.038	.907	1.000	-.002	.015	.015	.912	1.000
	CL	.005	.035	.033	.931	.784	.020	.042	.041	.896	.862	.001	.015	.015	.935	1.000
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Diagnostic sensitivity = .900					Diagnostic specificity = .900				
(.0, .0, .0)	FL	.004	.034	.033	.921	1.000	-.001	.016	.016	.938	1.000	-.001	.014	.014	.945	1.000
	CL	.002	.033	.032	.940	1.062	-.001	.016	.016	.939	1.000	-.001	.015	.014	.925	.871
(.0, .0, -.6)	FL	.004	.034	.033	.921	1.000	-.001	.016	.016	.937	1.000	-.001	.014	.014	.938	1.000
	CL	.002	.034	.033	.925	1.000	-.001	.017	.016	.940	0.886	.000	.015	.014	.922	.871
(.2, -.2, -.6)	FL	.007	.036	.033	.918	1.000	-.001	.018	.017	.916	1.000	-.001	.015	.015	.929	1.000
	CL	.008	.034	.034	.943	1.121	.001	.019	.018	.922	.898	.000	.015	.015	.939	1.000
(.6, -.6, -.6)	FL	.006	.033	.031	.909	1.000	-.001	.017	.017	.891	1.000	-.001	.015	.015	.904	1.000
	CL	.006	.035	.033	.923	.889	.006	.018	.017	.907	.892	.001	.014	.015	.941	1.148
(.8, -.8, -.8)	FL§	.005	.031	.029	.854	1.000	.000	.017	.016	.859	1.000	-.001	.015	.015	.865	1.000
	CL	.005	.034	.033	.925	.831	.008	.017	.017	.887	1.000	.001	.015	.015	.933	1.000

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method;
†: the non-convergence rate was 14.3%; §: the non-convergence rate was 23.9%.

Table S8: Summary of 1,000 simulations with 50 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall PPV and NPV. True values of PPV and NPV are (.600, .900) or (.692, .973).

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
$(\rho_{01}, \rho_{02}, \rho_{12})$		PPV = .600					NPV = .900				
(.0, .0, .0)	FL	.001	.062	.060	.924	1.000	-.003	.021	.020	.926	1.000
	CL	-.006	.063	.061	.933	.969	-.001	.021	.020	.936	1.000
(.0, .0 -.6)	FL	.001	.059	.056	.920	1.000	-.003	.021	.020	.926	1.000
	CL	-.003	.058	.056	.932	1.035	-.002	.021	.020	.936	1.000
(.2, -.2, -.6)	FL	.006	.060	.056	.910	1.000	-.004	.022	.020	.929	1.000
	CL	.007	.058	.055	.920	1.070	-.002	.021	.020	.930	1.098
(.6, -.6, -.6)	FL	.004	.050	.048	.915	1.000	-.003	.018	.017	.915	1.000
	CL	.013	.054	.049	.913	.857	.000	.019	.017	.924	.898
(.8, -.8, -.8)	FL†	.004	.042	.041	.890	1.000	-.002	.016	.015	.907	1.000
	CL	.015	.049	.044	.890	.735	.002	.018	.016	.897	.790
$(\rho_{01}, \rho_{02}, \rho_{12})$		PPV= .692					NPV = .973				
(.0, .0, .0)	FL	.000	.054	.052	.924	1.000	-.001	.007	.007	.939	1.000
	CL	-.003	.054	.052	.938	1.000	-.001	.007	.007	.945	1.000
(.0, .0 -.6)	FL	.000	.054	.051	.922	1.000	-.001	.007	.007	.939	1.000
	CL	-.001	.055	.052	.924	.964	-.001	.007	.007	.920	1.000
(.2, -.2, -.6)	FL	.003	.053	.050	.908	1.000	-.002	.008	.007	.919	1.000
	CL	.008	.050	.049	.935	1.124	-.001	.007	.007	.936	1.306
(.6, -.6, -.6)	FL	.003	.043	.041	.896	1.000	-.001	.006	.006	.901	1.000
	CL	.009	.045	.040	.895	.913	.001	.006	.006	.912	1.000
(.8, -.8, -.8)	FL§	.003	.037	.035	.853	1.000	-.001	.006	.005	.855	1.000
	CL	.008	.041	.034	.880	.814	.002	.006	.005	.911	1.000

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method;
†: the non-convergence rate was 14.3%; §: the non-convergence rate was 23.9%.

Table S9: Summary of 1,000 simulations with covariates and 30 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates for regression coefficients.

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
$(\rho_{01}, \rho_{02}, \rho_{12})$		β_{00}= .173					β_{01}= −1.295					β_{02} = .000				
(.0, .0, .0)	FL	.008	.412	.361	.901	1.000	.017	.600	.521	.899	1.000	-.013	.544	.464	.898	1.000
	CL	-.016	.437	.363	.876	.889	.034	.602	.521	.898	.993	-.013	.531	.461	.900	1.050
(.0, .0, -.6)	FL	.000	.403	.358	.870	1.000	.026	.593	.518	.869	1.000	-.012	.545	.462	.855	1.000
	CL	.018	.424	.366	.886	.903	.027	.602	.523	.886	.970	.004	.547	.460	.882	.993
(.2, -.2, -.6)	FL†	.009	.408	.357	.723	1.000	.001	.591	.527	.709	1.000	-.007	.545	.465	.707	1.000
	CL	-.010	.442	.358	.887	.852	.023	.617	.517	.879	.917	-.004	.544	.458	.894	1.004
(.6, -.6, -.6)	FL*	.006	.362	.318	.756	1.000	.008	.518	.465	.753	1.000	-.011	.479	.405	.739	1.000
	CL	-.005	.422	.357	.886	.736	.057	.618	.517	.888	.703	.019	.552	.459	.883	.753
(.8, -.8, -.8)	FL§	-.006	.318	.284	.789	1.000	-.009	.433	.371	.786	1.000	-.019	.428	.381	.771	1.000
	CL	-.022	.425	.366	.906	.560	.058	.579	.525	.901	.559	-.029	.506	.464	.910	.715

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method;
†: the non-convergence rate was 10.6%; *: the non-convergence rate was 10.1%; §: the non-convergence rate was 12.7%.

Table S9: Summary of 1,000 simulations with covariates and 30 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates for regression coefficients. **(continued)**

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
$(\rho_{01}, \rho_{02}, \rho_{12})$		$\beta_{10} = 1.712$					$\beta_{11} = -1.266$					$\beta_{12} = .000$				
(.0, .0, .0)	FL	.007	.329	.299	.919	1.000	-.014	.453	.421	.925	1.000	.000	.388	.368	.936	1.000
	CL	-.012	.339	.313	.917	.942	-.006	.461	.442	.931	.966	.003	.417	.386	.928	.866
(.0, .0, -.6)	FL	.007	.328	.296	.873	1.000	-.017	.450	.418	.895	1.000	-.005	.386	.366	.896	1.000
	CL	.005	.336	.313	.926	.953	.014	.463	.442	.934	.945	.016	.423	.385	.911	.833
(.2, -.2, -.6)	FL†	.019	.321	.291	.718	1.000	-.023	.431	.412	.729	1.000	-.001	.385	.360	.727	1.000
	CL	.013	.347	.314	.917	.856	-.006	.475	.441	.922	.823	.005	.413	.385	.925	.869
(.6, -.6, -.6)	FL*	.018	.315	.285	.758	1.000	-.017	.423	.344	.760	1.000	-.001	.390	.346	.750	1.000
	CL	.034	.324	.314	.938	.945	.050	.464	.445	.928	.831	.014	.418	.391	.928	.871
(.8, -.8, -.8)	FL§	.018	.304	.274	.788	1.000	-.024	.403	.382	.796	1.000	-.022	.375	.346	.789	1.000
	CL	.047	.335	.314	.924	.823	.052	.478	.441	.915	.711	-.015	.405	.385	.941	.857
$(\rho_{01}, \rho_{02}, \rho_{12})$		$\beta_{20} = 1.912$					$\beta_{21} = 1.263$					$\beta_{22} = .000$				
(.0, .0, .0)	FL	-.007	.327	.292	.910	1.000	-.001	.471	.435	.921	1.000	-.007	.432	.378	.911	1.000
	CL	.017	.329	.297	.908	.988	.000	.472	.442	.928	.996	-.024	.400	.382	.938	1.166
(.0, .0, -.6)	FL	-.005	.323	.293	.875	1.000	.015	.485	.437	.878	1.000	-.008	.408	.379	.903	1.000
	CL	.004	.326	.293	.915	.982	-.020	.477	.436	.919	1.034	.005	.398	.377	.935	1.051
(.2, -.2, -.6)	FL†	.017	.311	.285	.723	1.000	.023	.468	.444	.726	1.000	-.012	.393	.363	.734	1.000
	CL	.015	.328	.299	.924	.899	-.004	.478	.441	.923	.959	-.017	.397	.384	.925	.980
(.6, -.6, -.6)	FL*	.012	.315	.284	.756	1.000	.024	.460	.423	.750	1.000	-.009	.400	.359	.766	1.000
	CL	.029	.327	.297	.915	.928	-.017	.475	.442	.928	.938	-.007	.419	.387	.917	.911
(.8, -.8, -.8)	FL§	.018	.305	.279	.788	1.000	.011	.432	.402	.781	1.000	-.014	.383	.346	.790	1.000
	CL	.065	.333	.299	.912	.839	-.031	.480	.442	.920	.810	-.009	.422	.385	.919	.824

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method;
†: the non-convergence rate was 10.6%; *: the non-convergence rate was 10.1%; §: the non-convergence rate was 12.7%.

Table S10: Summary of 1,000 simulations with covariates and 50 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall disease prevalence and diagnostic test sensitivity and specificity.

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
(ρ_{01}, ρ_{02}, ρ_{12})		β_{00}= .173					β_{01}= −1.295					β_{02} = .000				
(.0, .0, .0)	FL	-.011	.311	.287	.928	1.000	.034	.436	.413	.935	1.000	.007	.386	.363	.925	1.000
	CL	-.017	.302	.287	.934	1.060	.028	.425	.409	.938	1.052	.008	.396	.357	.913	.950
(.0, .0, -.6)	FL	-.010	.305	.288	.933	1.000	.029	.431	.432	.934	1.000	.012	.390	.363	.920	1.000
	CL	.003	.322	.286	.908	.897	-.008	.451	.410	.913	.913	-.002	.401	.357	.908	.946
(.2, -.2, -.6)	FL	-.012	.310	.309	.911	1.000	.027	.447	.437	.911	1.000	.008	.404	.398	.902	1.000
	CL	-.001	.312	.288	.905	.987	.007	.446	.414	.915	1.004	.004	.394	.363	.919	1.051
(.6, -.6, -.6)	FL	-.004	.282	.278	.861	1.000	.017	.402	.399	.852	1.000	.014	.365	.358	.852	1.000
	CL	.017	.313	.286	.929	.812	.006	.455	.411	.912	.781	.007	.374	.357	.928	.952
(.8, -.8, -.8)	FL	-.014	.252	.269	.897	1.000	.008	.353	.386	.907	1.000	-.016	.327	.339	.883	1.000
	CL	-.013	.312	.290	.926	.652	.021	.436	.417	.932	.656	.008	.402	.365	.932	.662

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method.

Table S10: Summary of 1,000 simulations with covariates and 50 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall disease prevalence and diagnostic test sensitivity and specificity. **(continued)**

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
$(\rho_{01}, \rho_{02}, \rho_{12})$		$\beta_{10} = 1.712$					$\beta_{11} = -1.266$					$\beta_{12} = .000$				
(.0, .0, .0)	FL	.001	.245	.231	.937	1.000	-.002	.349	.324	.924	1.000	-.016	.310	.282	.922	1.000
	CL	.005	.273	.249	.924	.805	.006	.365	.348	.929	.914	-.012	.317	.303	.931	.956
(.0, .0, -.6)	FL	.002	.248	.229	.921	1.000	-.002	.357	.322	.922	1.000	-.015	.308	.280	.931	1.000
	CL	-.005	.253	.248	.946	.961	-.003	.363	.349	.931	.967	-.004	.328	.303	.922	.882
(.2, -.2, -.6)	FL	.014	.249	.247	.909	1.000	-.013	.359	.348	.905	1.000	-.017	.313	.303	.908	1.000
	CL	-.001	.265	.247	.935	.883	.020	.364	.349	.942	.973	.004	.309	.304	.944	1.026
(.6, -.6, -.6)	FL	.004	.246	.248	.850	1.000	.001	.343	.349	.853	1.000	-.011	.303	.304	.855	1.000
	CL	.058	.252	.248	.933	.953	.013	.357	.350	.940	.923	.004	.311	.303	.933	.949
(.8, -.8, -.8)	FL	.002	.240	.243	.889	1.000	.001	.330	.344	.897	1.000	-.019	.299	.300	.889	1.000
	CL	.053	.253	.248	.940	.900	.027	.358	.349	.928	.850	-.003	.326	.305	.936	.841
$(\rho_{01}, \rho_{02}, \rho_{12})$		$\beta_{20} = 1.912$					$\beta_{21} = 1.263$					$\beta_{22} = .000$				
(.0, .0, .0)	FL	.002	.242	.230	.932	1.000	.001	.359	.341	.933	1.000	-.003	.313	.295	.938	1.000
	CL	.001	.241	.233	.942	1.008	-.006	.361	.343	.936	.989	-.015	.323	.298	.923	.939
(.0, .0, -.6)	FL	-.002	.246	.230	.924	1.000	.008	.371	.340	.920	1.000	-.003	.316	.295	.926	1.000
	CL	.007	.250	.234	.927	.968	.002	.365	.344	.930	1.033	.002	.320	.298	.922	.975
(.2, -.2, -.6)	FL	.018	.246	.249	.911	1.000	.014	.371	.367	.909	1.000	-.001	.321	.318	.906	1.000
	CL	.016	.242	.233	.942	1.033	-.001	.358	.345	.938	1.074	-.002	.311	.299	.941	1.065
(.6, -.6, -.6)	FL	.019	.247	.249	.846	1.000	.002	.358	.365	.856	1.000	-.006	.307	.318	.858	1.000
	CL	.046	.251	.233	.927	.968	-.012	.368	.344	.929	.946	-.009	.301	.298	.946	1.040
(.8, -.8, -.8)	FL	.022	.233	.244	.898	1.000	-.004	.336	.360	.912	1.000	-.010	.296	.312	.907	1.000
	CL	.058	.240	.234	.940	.943	-.022	.344	.346	.945	.954	-.001	.321	.301	.923	.850

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method.

Table S11: Summary of 1,000 simulations with data generated from multivariate t distribution with 4 d.f. and 8 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall disease prevalence and diagnostic test sensitivity and specificity.

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Sensitivity = .600					Specificity = .900				
(.0, .0, .0)	FL	.025	.112	.105	.892	1.000	.005	.116	.115	.915	1.000	-.007	.049	.047	.916	1.000
	CL	.023	.107	.083	.805	1.096	-.004	.115	.104	.865	1.017	-.009	.049	.044	.886	1.000
(.0, .0, -.6)	FL	.025	.112	.106	.814	1.000	.005	.118	.116	.821	1.000	-.009	.051	.049	.826	1.000
	CL	.026	.109	.085	.804	1.056	-.001	.114	.104	.878	1.071	-.011	.051	.045	.892	1.000
(.2, -.2, -.6)	FL†	.024	.098	.101	.363	1.000	.005	.113	.117	.381	1.000	-.009	.048	.049	.377	1.000
	CL	.021	.109	.085	.800	.808	-.001	.116	.104	.860	.949	-.009	.048	.044	.887	1.000
(.6, -.6, -.6)	FL‡	.018	.092	.095	.441	1.000	.005	.107	.114	.448	1.000	-.008	.046	.047	.451	1.000
	CL	.017	.106	.085	.789	.753	.011	.114	.102	.868	.881	-.007	.048	.044	.897	.918
(.8, -.8, -.8)	FL§	.013	.080	.086	.584	1.000	.005	.108	.113	.577	1.000	-.009	.045	.047	.593	1.000
	CL	.019	.110	.083	.792	.529	.016	.113	.101	.856	.913	-.004	.044	.040	.875	1.046
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Sensitivity = .900					Specificity = .900				
(.0, .0, .0)	FL	.025	.112	.105	.891	1.000	-.003	.052	.051	.897	1.000	-.007	.049	.047	.914	1.000
	CL	.026	.111	.088	.811	1.018	-.011	.053	.050	.889	.963	-.010	.049	.044	.889	1.000
(.0, .0, -.6)	FL	.026	.112	.104	.742	1.000	-.004	.053	.052	.777	1.000	-.009	.050	.047	.770	1.000
	CL	.024	.106	.088	.796	1.116	-.009	.057	.048	.875	.865	-.012	.052	.045	.878	.925
(.2, -.2, -.6)	FL*	.025	.104	.103	.281	1.000	-.003	.047	.052	.288	1.000	-.008	.047	.049	.284	1.000
	CL	.025	.112	.087	.787	.862	-.007	.053	.048	.885	.786	-.008	.046	.044	.895	1.044
(.6, -.6, -.6)	FL$^{\mp}$	.018	.094	.089	.385	1.000	-.004	.051	.051	.399	1.000	-.008	.047	.045	.396	1.000
	CL	.024	.116	.086	.768	.657	-.003	.053	.046	.847	.926	-.007	.049	.043	.868	.920
(.8, -.8, -.8)	FL*	.016	.085	.086	.508	1.000	-.002	.049	.050	.514	1.000	-.009	.048	.047	.508	1.000
	CL	.027	.114	.086	.783	.556	.002	.050	.045	.867	.960	-.007	.046	.042	.871	1.089

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method;
†: the non-convergence rate was 25.4%; ‡: the non-convergence rate was 24.8%;
§: the non-convergence rate was 21.3%; *: the non-convergence rate was 28.9%;
$^{\mp}$: the non-convergence rate was 26.3%; *: the non-convergence rate was 27.6%.

Table S12: Summary of 1,000 simulations with data generated from multivariate t distribution with 4 d.f. and 8 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall PPV and NPV. True values of PPV and NPV are (.600, .900) or (.692, .973).

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
$(\rho_{01}, \rho_{02}, \rho_{12})$		PPV = .600					NPV = .900				
(.0, .0, .0)	FL	-.001	.174	.172	.867	1.000	-.008	.078	.072	.888	1.000
	CL	-.010	.172	.146	.852	1.023	-.008	.074	.061	.860	1.111
(.0, .0, -.6)	FL	-.003	.168	.162	.805	1.000	-.008	.077	.071	.824	1.000
	CL	-.007	.163	.134	.862	1.062	-.009	.076	.061	.877	1.026
(.2, -.2, -.6)	FL†	.000	.153	.149	.363	1.000	-.015	.065	.063	.358	1.000
	CL	-.009	.155	.135	.857	.974	-.015	.072	.064	.869	.815
(.6, -.6, -.6)	FL‡	-.002	.137	.132	.434	1.000	-.010	.056	.053	.436	1.000
	CL	-.004	.147	.121	.857	.869	-.008	.063	.049	.864	.790
(.8, -.8, -.8)	FL§	.597	.117	.118	.574	1.000	-.005	.043	.043	.574	1.000
	CL	.605	.135	.102	.823	.751	-.007	.062	.057	.818	.481
$(\rho_{01}, \rho_{02}, \rho_{12})$		PPV= .692					NPV = .973				
(.0, .0, .0)	FL	-.009	.157	.151	.863	1.000	-.008	.032	.028	.868	1.000
	CL	-.014	.154	.133	.865	1.039	-.012	.037	.030	.892	.748
(.0, .0, -.6)	FL	-.010	.157	.146	.722	1.000	-.009	.032	.028	.752	1.000
	CL	-.015	.148	.132	.868	1.125	-.009	.032	.025	.878	1.000
(.2, -.2, -.6)	FL*	-.006	.142	.133	.255	1.000	-.007	.026	.024	.267	1.000
	CL	-.010	.140	.124	.889	1.029	-.009	.031	.025	.881	.703
(.6, -.6, -.6)	FL$^{\mp}$	-.008	.124	.108	.373	1.000	-.004	.021	.019	.388	1.000
	CL	-.004	.132	.103	.830	.882	-.006	.026	.020	.845	.459
(.8, -.8, -.8)	FL*	-.004	.103	.098	.518	1.000	-.002	.015	.015	.521	1.000
	CL	.000	.121	.091	.829	.725	-.004	.024	.016	.846	.391

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method;
†: the non-convergence rate was 25.4%; ‡: the non-convergence rate was 24.8%;
§: the non-convergence rate was 21.3%; *: the non-convergence rate was 28.9%;
$^{\mp}$: the non-convergence rate was 26.3%; *: the non-convergence rate was 27.6%.

Table S13: Summary of 1,000 simulations with data generated from multivariate t distribution with d.f.=4 and 30 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall disease prevalence and diagnostic test sensitivity and specificity.

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Diagnostic sensitivity = .600					Diagnostic specificity = .900				
(.0, .0, .0)	FL	.008	.053	.054	.947	1.000	.003	.059	.060	.938	1.000	-.002	.023	.024	.949	1.000
	CL	.008	.054	.052	.920	.963	-.002	.061	.059	.919	.936	-.001	.023	.023	.939	1.000
(.0, .0, -.6)	FL	.008	.053	.055	.945	1.000	.003	.059	.061	.935	1.000	-.003	.023	.024	.950	1.000
	CL	.005	.054	.051	.912	.963	-.005	.061	.059	.926	.936	-.002	.023	.024	.938	1.000
(.2, -.2, -.6)	FL	.010	.056	.054	.901	1.000	.004	.060	.062	.911	1.000	-.003	.023	.024	.917	1.000
	CL	.007	.053	.052	.918	1.116	.003	.061	.059	.928	.967	-.001	.024	.023	.925	.918
(.6, -.6, -.6)	FL	.010	.050	.050	.895	1.000	.004	.060	.061	.886	1.000	-.003	.022	.024	.914	1.000
	CL	.008	.053	.052	.930	.890	.016	.057	.058	.916	1.108	.001	.023	.023	.926	.915
(.8, -.8, -.8)	FL	.010	.047	.047	.784	1.000	.007	.060	.060	.778	1.000	-.005	.023	.024	.792	1.000
	CL	.009	.056	.053	.910	.704	.022	.058	.057	.900	1.070	.001	.023	.022	.914	1.000
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Diagnostic sensitivity = .900					Diagnostic specificity = .900				
(.0, .0, .0)	FL	.008	.053	.054	.946	1.000	.001	.025	.026	.938	1.000	-.002	.023	.024	.949	1.000
	CL	.008	.052	.052	.915	1.039	-.001	.025	.026	.942	1.000	-.003	.023	.024	.944	1.000
(.0, .0, -.6)	FL	.008	.053	.054	.944	1.000	.001	.025	.026	.938	1.000	-.002	.023	.024	.944	1.000
	CL	.009	.056	.052	.910	.896	-.001	.026	.026	.920	.925	-.003	.023	.024	.948	1.000
(.2, -.2, -.6)	FL	.010	.056	.054	.850	1.000	.001	.026	.027	.863	1.000	-.003	.023	.024	.872	1.000
	CL	.011	.055	.053	.923	1.037	.002	.025	.025	.933	1.082	-.002	.023	.023	.944	1.000
(.6, -.6, -.6)	FL	.009	.051	.050	.805	1.000	.001	.025	.026	.801	1.000	-.003	.022	.024	.818	1.000
	CL	.006	.054	.052	.917	.892	.007	.024	.024	.910	1.085	.001	.023	.023	.927	.915
(.8, -.8, -.8)	FL†	.007	.047	.047	.660	1.000	.002	.025	.026	.649	1.000	-.003	.023	.024	.669	1.000
	CL	.012	.056	.053	.930	.704	.010	.024	.023	.882	1.085	.000	.023	.023	.931	1.000
(.0,.0,-.6),(.6,-.6,-.6)	FL$^{\pm}$	.032	.089	.076	.759	1.000	-.004	.040	.040	.750	1.000	-.007	.040	.034	.769	1.000
	CL	.008	.053	.051	.930	2.820	-.003	.027	.027	.945	2.195	-.003	.023	.024	.946	3.025

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method;
†: the non-convergence rate was 10.6%; $^{\pm}$: the non-convergence rate was 48.1%.

Table S14: Summary of 1,000 simulations with data generated from multivariate t distribution with d.f.= 4 and 30 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall PPV and NPV. True values of PPV and NPV are (.600, .900) or (.692, .973).

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
(ρ_{01}, ρ_{02}, ρ_{12})		PPV = .600					NPV = .900				
(.0, .0, .0)	FL	.003	.096	.098	.931	1.000	-.005	.034	.035	.937	1.000
	CL	.002	.096	.093	.929	1.000	-.006	.035	.033	.929	.944
(.0, .0, -.6)	FL	.001	.090	.091	.930	1.000	-.005	.034	.034	.934	1.000
	CL	-.006	.094	.087	.914	.917	-.005	.034	.032	.935	1.000
(.2, -.2, -.6)	FL	.003	.091	.086	.873	1.000	-.006	.034	.033	.903	1.000
	CL	.004	.086	.084	.932	1.120	-.004	.032	.031	.929	1.129
(.6, -.6, -.6)	FL	.005	.077	.073	.865	1.000	-.004	.028	.027	.887	1.000
	CL	.015	.078	.072	.904	.975	-.011	.030	.027	.915	.871
(.8, -.8, -.8)	FL	.004	.063	.062	.761	1.000	-.004	.023	.023	.787	1.000
	CL	.019	.074	.063	.876	.725	.001	.028	.025	.918	.675
(ρ_{01}, ρ_{02}, ρ_{12})		PPV= .692					NPV = .973				
(.0, .0, .0)	FL	.001	.084	.084	.927	1.000	-.002	.012	.012	.920	1.000
	CL	-.003	.081	.081	.937	1.075	-.002	.011	.012	.940	1.190
(.0, .0, -.6)	FL	-.001	.083	.083	.922	1.000	-.002	.012	.012	.923	1.000
	CL	-.003	.085	.080	.929	.953	-.003	.012	.012	.940	1.000
(.2, -.2, -.6)	FL	.001	.082	.077	.829	1.000	-.002	.012	.011	.850	1.000
	CL	.003	.080	.074	.916	1.051	-.002	.011	.011	.944	1.190
(.6, -.6, -.6)	FL	.002	.066	.062	.769	1.000	-.001	.009	.009	.795	1.000
	CL	.005	.071	.059	.882	.864	.001	.010	.009	.903	.810
(.8, -.8, -.8)	FL†	.001	.053	.051	.648	1.000	.000	.008	.008	.655	1.000
	CL	.013	.062	.051	.867	.731	.001	.009	.008	.898	.790
(.0,.0,-.6),(.6,-.6,-.6)	FL $^{\pm}$	.011	.116	.108	.724	1.000	-.008	.023	.020	.753	1.000
	CL	-.003	.082	.079	.932	2.001	-.003	.012	.012	.933	3.674

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method;
†: the non-convergence rate was 10.6%; $^{\pm}$: the non-convergence rate was 48.1%.

Table S15: Summary of 1,000 simulations with data generated from multivariate t distribution with 4 d.f. and 50 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall disease prevalence and diagnostic test sensitivity and specificity.

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Diagnostic sensitivity = .600					Diagnostic specificity = .900				
(.0, .0, .0)	FL	.006	.043	.042	.944	1.000	.000	.047	.047	.940	1.000	-.001	.018	.018	.946	1.000
	CL	.006	.043	.041	.930	1.000	-.001	.046	.046	.944	1.044	-.002	.018	.018	.945	1.000
(.0, .0, -.6)	FL	.006	.043	.042	.944	1.000	.001	.047	.047	.936	1.000	-.001	.018	.018	.957	1.000
	CL	.007	.044	.041	.928	.955	-.001	.046	.046	.936	1.044	-.002	.018	.018	.959	1.000
(.2, -.2, -.6)	FL	.007	.043	.041	.941	1.000	.001	.047	.048	.945	1.000	-.001	.018	.018	.950	1.000
	CL	.010	.043	.042	.941	1.000	.006	.046	.046	.936	1.044	-.001	.018	.018	.942	1.000
(.6, -.6, -.6)	FL	.006	.039	.038	.941	1.000	.001	.048	.047	.936	1.000	-.001	.018	.018	.941	1.000
	CL	.006	.040	.041	.948	.951	.015	.046	.045	.917	1.089	.001	.018	.018	.932	1.000
(.8, -.8, -.8)	FL	.006	.036	.036	.905	1.000	.002	.048	.047	.899	1.000	-.002	.018	.018	.910	1.000
	CL	.007	.041	.041	.945	.771	.022	.046	.045	.903	1.089	.001	.017	.017	.949	1.121
(ρ_{01}, ρ_{02}, ρ_{12})		Disease prevalence = .200					Diagnostic sensitivity = .900					Diagnostic specificity = .900				
(.0, .0, .0)	FL	.006	.043	.042	.943	1.000	.001	.020	.020	.942	1.000	-.001	.018	.018	.945	1.000
	CL	.007	.040	.042	.948	1.156	-.002	.020	.021	.951	1.000	-.001	.018	.018	.942	1.000
(.0, .0, -.6)	FL	.006	.043	.042	.943	1.000	.001	.020	.020	.943	1.000	-.001	.018	.018	.957	1.000
	CL	.006	.042	.041	.929	1.048	-.001	.020	.020	.949	1.000	-.001	.018	.018	.957	1.000
(.2, -.2, -.6)	FL	.007	.044	.041	.919	1.000	.001	.020	.021	.922	1.000	-.001	.018	.018	.938	1.000
	CL	.008	.042	.041	.932	1.098	.003	.020	.020	.916	1.000	-.002	.018	.018	.949	1.000
(.6, -.6, -.6)	FL	.006	.039	.038	.914	1.000	.000	.020	.020	.923	1.000	-.001	.018	.018	.919	1.000
	CL	.006	.041	.041	.942	.905	.007	.019	.019	.898	1.108	.000	.017	.018	.950	1.121
(.8, -.8, -.8)	FL	.005	.037	.036	.807	1.000	.001	.020	.020	.807	1.000	-.001	.018	.018	.811	1.000
	CL	.007	.041	.041	.942	.814	.011	.018	.018	.865	1.235	.000	.017	.017	.942	1.121

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method.

Table S16: Summary of 1,000 simulations with data generated from multivariate t distribution with 4 d.f. and 50 studies: bias (BIAS), standard error (SE), model-based standard error (MBSE), coverage probability (CP) and relative efficiency (RE) of estimates of overall PPV and NPV. True values of PPV and NPV are (.600, .900) or (.692, .973).

		BIAS	SE	MBSE	CP	RE	BIAS	SE	MBSE	CP	RE
(ρ_{01}, ρ_{02}, ρ_{12})		PPV = .600					NPV = .900				
(.0, .0, .0)	FL	.001	.078	.076	.914	1.000	-.004	.027	.026	.940	1.000
	CL	.000	.078	.076	.931	1.000	-.004	.027	.026	.937	1.000
(.0, .0, -.6)	FL	.002	.072	.071	.931	1.000	-.004	.026	.026	.943	1.000
	CL	-.001	.072	.070	.937	1.000	-.005	.027	.026	.940	.927
(.2, -.2, -.6)	FL	.003	.070	.067	.925	1.000	-.004	.025	.025	.936	1.000
	CL	.010	.068	.066	.932	1.060	-.005	.026	.025	.928	.925
(.6, -.6, -.6)	FL	.004	.059	.057	.916	1.000	-.003	.021	.021	.941	1.000
	CL	.014	.061	.057	.919	.936	.000	.023	.021	.927	.834
(.8, -.8, -.8)	FL	.004	.049	.047	.885	1.000	-.002	.017	.017	.911	1.000
	CL	.019	.056	.050	.895	.766	.001	.021	.019	.931	.655
(ρ_{01}, ρ_{02}, ρ_{12})		PPV= .692					NPV = .973				
(.0, .0, .0)	FL	.001	.067	.066	.922	1.000	-.001	.009	.009	.941	1.000
	CL	.002	.064	.065	.950	1.096	-.002	.009	.009	.947	1.000
(.0, .0, -.6)	FL	.001	.066	.065	.931	1.000	-.001	.009	.009	.941	1.000
	CL	.001	.063	.064	.952	1.098	-.001	.009	.009	.936	1.000
(.2, -.2, -.6)	FL	.002	.063	.060	.910	1.000	-.001	.009	.008	.927	1.000
	CL	.002	.061	.059	.938	1.067	.000	.008	.008	.935	1.266
(.6, -.6, -.6)	FL	.004	.050	.048	.893	1.000	-.001	.007	.007	.923	1.000
	CL	.007	.052	.048	.917	.925	-.001	.007	.007	.913	1.000
(.8, -.8, -.8)	FL	.003	.040	.039	.794	1.000	.000	.006	.006	.820	1.000
	CL	.010	.050	.040	.879	.640	.002	.006	.006	.905	1.000

FL: Full likelihood method based on the hybrid GLMM; CL: Composite likelihood method.

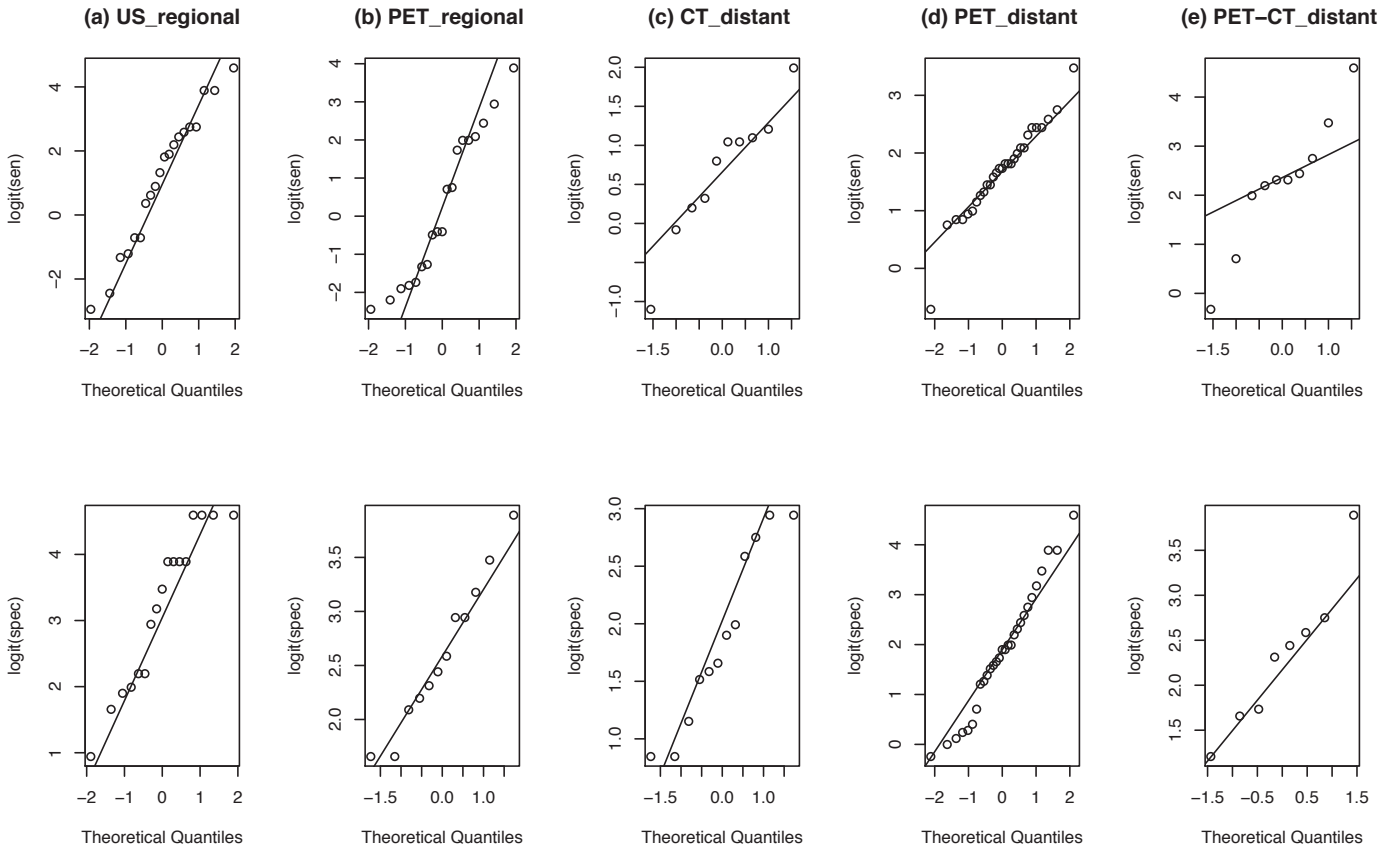

Figure S3: Upper panel: normal Q-Q plots with respect to sensitivity (logit scale) in each stratum; Lower panel: normal Q-Q plots with respect to specificity (logit scale) in each stratum.

Section 6: R program for the composite likelihood method and SAS program for the full likelihood method and an example

```
####################
## R program
####################

### functions to compute the score functions w.r.t theta0, theta1 and theta2
## density function of logit-normal
dlogitnorm = function(p, mu, tau2){
(2*pi*tau2)^(-1/2)*exp(-(qlogis(p)-mu)^2/(2*tau2))/(p*(1-p))
}

integrand1 = function(n,y, mypar2, p.grid){
dbinom(y, size=n, prob=p.grid)*dlogitnorm(p.grid, mypar2[1], mypar2[2])
}

integrand2 = function(n,y,mypar2, p.grid){
dbinom(y, size=n, prob=p.grid)*dlogitnorm(p.grid, mypar2[1], mypar2[2])*2*(qlogis(p.grid)-mypar2[1])/(2*mypar2[2])
}

integrand3 = function(n,y,mypar2, p.grid){
dbinom(y, size=n, prob=p.grid)*dlogitnorm(p.grid, mypar2[1], mypar2[2])*(-1/(2*mypar2[2])+(qlogis(p.grid)-mypar2[1])^2/(2*mypar2[2]^2))
}

### R library for use of "integrate" and "glmmML" functions
library(stats)
library(glmmML)

### Example: dataset are collected from the distant metastais with the computed tomography (CT) diagnsotic test (Xing,2011) in Section 4
estim = estim.orig = mbse.orig = matrix(NA,nrow=6,ncol=1)
mySandwich = matrix(NA,nrow=6,ncol=6)

id = c(23,24,27,29,32,36,37,26,28,30,31,38)
```

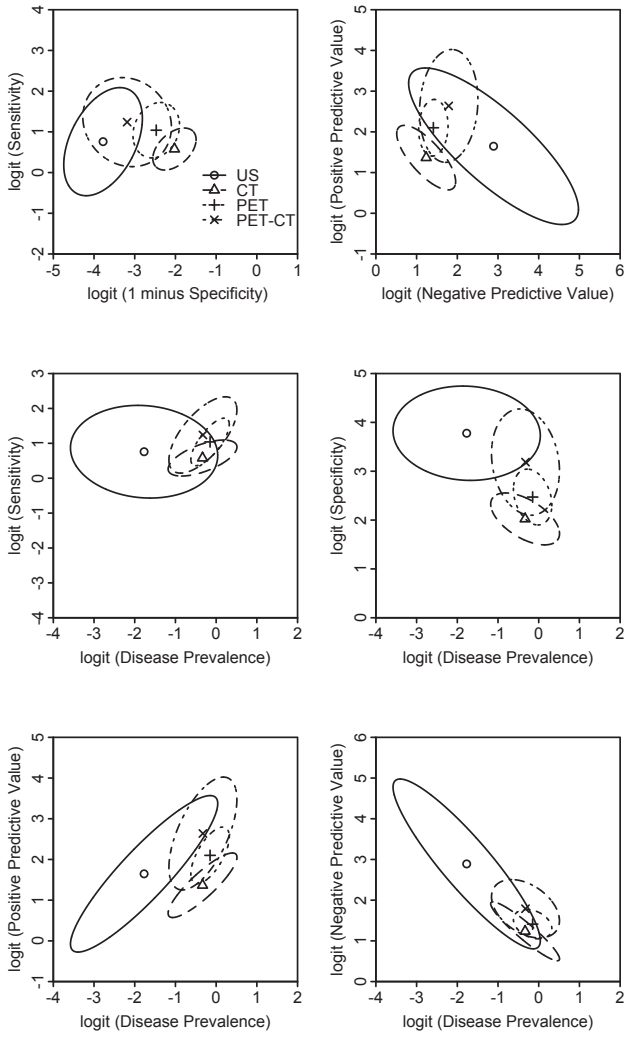

Figure S4: Summary points and 95% confidence regions of logit(sensitivity) versus logit(1-minus-specificity) (upper left panel), logit(PPV) versus logit(NPV) (upper right panel), logit(sensitivity) and logit(specificity) versus logit(metastasis prevalence) (middle panels), logit(predictive values) versus logit(metastasis prevalence) (lower panels) for four diagnostic imaging modalities. Filled circle: summary point; solid line: boundary of 95% confidence region for the summary point.

```
Nt = c(151,89,104,34,106,115,250,76,18,103,64,74)
PiY = c(NA,NA,NA,NA,NA,NA,NA,37,9,44,46,15)
Nd = c(0,4,87,5,59,13,89,37,9,44,46,15)
SeY = c(0,4,50,4,41,9,66,20,7,21,35,4)
Nn = c(151,85,17,29,47,102,161,39,9,59,18,59)
SpY = c(124,65,12,28,44,85,141,33,8,56,13,55)
mydat1 = data.frame(cbind(id,Nt, PiY, Nd, SeY, Nn, SpY))
names(mydat1) = c("id", "Nt","PiY", "Nd","SeY","Nn","SpY")
mydat2 = mydat1[is.na(mydat1$PiY)==FALSE, ]## cohort studies only

m = nrow(mydat1) ## number of all studies
m2 = nrow(mydat2) ## number of the cohort studies
m1 = m-m2 ## number of the rest of case-control studies

### The method of the composite likelihood in Section 2
## 1.1 point estimate: fit GLMM model(using Gauss-Hermite quadrature method with points 8)
fit.PiY = glmmML(cbind(PiY, Nt-PiY)~1, data = mydat2, cluster = id, method= "ghq", n.points=8,
control=list(epsilon=1e-08, maxit=50000,trace=FALSE))
fit.SeY = glmmML(cbind(SeY, Nd-SeY)~1, data = mydat1, cluster = id, method= "ghq", n.points=8,
control=list(epsilon=1e-08, maxit=50000,trace=FALSE))
fit.SpY = glmmML(cbind(SpY, Nn-SpY)~1, data = mydat1, cluster = id, method= "ghq", n.points=8,
control=list(epsilon=1e-08, maxit=50000,trace=FALSE))

## Logit scale for prevalence, sensitivity and specificity
```

```
estim[c(1: 2), 1] = c(as.numeric(fit.PiY$coefficients), (fit.PiY$sigma)^2)
estim[c(3: 4), 1] = c(as.numeric(fit.SeY$coefficients), (fit.SeY$sigma)^2)
estim[c(5: 6), 1] = c(as.numeric(fit.SpY$coefficients), (fit.SpY$sigma)^2)

## translate to the original scale for prevalence, sensitivity and specificity
estim.orig[c(1: 2), 1] = c(plogis(estim[1, 1]), estim[2, 1])
estim.orig[c(3: 4), 1] = c(plogis(estim[3, 1]), estim[4, 1])
estim.orig[c(5: 6), 1] = c(plogis(estim[5, 1]), estim[6, 1])

## 1.2 The variance estimate: using the Sandwich method
## calculate I00.hat, I11.hat and I22.hat
I00.hat = solve(m2*fit.PiY$variance)
I11.hat = solve(m*fit.SeY$variance)
I22.hat = solve(m*fit.SpY$variance)

## calculation of score function (study-specific) w.r.t theta0
int1 = int2  = int3 = rep(NA, length=m2)
est0 = estim[c(1: 2), 1] ##plug in the point estimate based on disease prevalence
for(i in 1: m2){
int1[i] = integrate(integrand1, lower=0, upper=1, n=mydat2$Nt[i], mypar2=est0, y=mydat2$PiY[i])$value
int2[i] = integrate(integrand2, lower=0, upper=1, n=mydat2$Nt[i], mypar2=est0, y=mydat2$PiY[i])$value
int3[i] = integrate(integrand3, lower=0, upper=1, n=mydat2$Nt[i], mypar2=est0, y=mydat2$PiY[i])$value
}
## derivation for PiY w.r.t beta0 and tau0^2 based on the prevalence data
derivePiY.mu = int2/int1
derivePiY.tau2 = int3/int1
B.PiY = cbind(derivePiY.mu, derivePiY.tau2)

## calculation of score function (study-specific) wrpt theta1
int1 = int2  = int3 = rep(NA, length=m)
est1 = estim[c(3: 4), 1] ##plug in the point estimate based on sensitivity
for(i in 1: m){
int1[i] = integrate(integrand1, lower=0, upper=1, n=mydat1$Nd[i], mypar2=est1, y=mydat1$SeY[i])$value
int2[i] = integrate(integrand2, lower=0, upper=1, n=mydat1$Nd[i], mypar2=est1, y=mydat1$SeY[i])$value
int3[i] = integrate(integrand3, lower=0, upper=1, n=mydat1$Nd[i], mypar2=est1, y=mydat1$SeY[i])$value
}
## derivation for SeY w.r.t beta1 and tau1^2 based on the sensitivity data
deriveSeY.mu = int2/int1
deriveSeY.tau2 = int3/int1
B.SeY = cbind(deriveSeY.mu, deriveSeY.tau2)
B.SeY.del = B.SeY[-c(1:m1), ] ## delete the first m1 studies

## score function (study-specific) wrpt theta2
int1 = int2  = int3 = rep(NA, length=m)
est2 = estim[c(5: 6), 1] ##plug in the point estimate based on specificity
for(i in 1: m){
int1[i] = integrate(integrand1, lower=0, upper=1, n=mydat1$Nn[i], mypar2=est2, y=mydat1$SpY[i])$value
int2[i] = integrate(integrand2, lower=0, upper=1, n=mydat1$Nn[i], mypar2=est2, y=mydat1$SpY[i])$value
int3[i] = integrate(integrand3, lower=0, upper=1, n=mydat1$Nn[i], mypar2=est2, y=mydat1$SpY[i])$value
}
## derivation for SpY w.r.t beta2 and tau2^2 based on the specificity data
deriveSpY.mu = int2/int1
deriveSpY.tau2 = int3/int1
B.SpY = cbind(deriveSpY.mu, deriveSpY.tau2)
B.SpY.del = B.SpY[-c(1:m1), ] ## delete the first m1 studies

## calculate I01.hat, I02.hat and I12.hat
I01.hat = t(B.PiY)%*%B.SeY.del/m2
I02.hat = t(B.PiY)%*%B.SpY.del/m2
I12.hat = t(B.SeY)%*%B.SpY/m

myoff.diag01 = solve(I00.hat)%*%I01.hat%*%solve(I11.hat)/m
myoff.diag02 = solve(I00.hat)%*%I02.hat%*%solve(I22.hat)/m
myoff.diag12 = solve(I11.hat)%*%I12.hat%*%solve(I22.hat)/m
myupper = cbind(fit.PiY$variance, sqrt(m/m2)*(myoff.diag01), sqrt(m/m2)*(myoff.diag02))
mymiddle = cbind(sqrt(m/m2)*t(myoff.diag01), fit.SeY$variance, (myoff.diag12))
mylower = cbind(sqrt(m/m2)*t(myoff.diag02), t(myoff.diag12), fit.SpY$variance)
myV = rbind(myupper, mymiddle, mylower)
mySandwich = myV

## calculate the model-based standard error for prevalence, sensitivity and specificity using delta method
pi.mbse = (estim.orig[1, 1]*(1-estim.orig[1, 1]))*sqrt(diag(myV)[1])
se.mbse = (estim.orig[3, 1]*(1-estim.orig[3, 1]))*sqrt(diag(myV)[3])
sp.mbse = (estim.orig[5, 1]*(1-estim.orig[5, 1]))*sqrt(diag(myV)[5])
s1.2.mbse = sqrt(diag(myV)[2])
s2.2.mbse = sqrt(diag(myV)[4])
s3.2.mbse = sqrt(diag(myV)[6])
mbse.orig = c(pi.mbse, s1.2.mbse, se.mbse, s2.2.mbse, sp.mbse, s3.2.mbse)



######################
## SAS program
######################

/*The method of the full likelihood function in Section 2*/
```

```
/*Input the data*/
data CTdistant;
input  id Nt PiY Nd SeY Nn SpY design;
datalines;
23 151  .  0   0 151 124 0
24  89  .  4   4  85  65 0
27 104  . 87  50  17  12 0
29  34  .  5   4  29  28 0
32 106  . 59  41  47  44 0
36 115  . 13   9 102  85 0
37 250  . 89  66 161 141 0
26  76  37 37  20  39  33 1
28  18   9  9   7   9   8 1
30 103  44 44  21  59  56 1
31  64  46 46  35  18  13 1
38  74  15 15   4  59  55 1
run;

data tnmeta;
set CTdistant;
keep id Y ntp nfp ntn nfn design;
ntp = SeY; nfn = Nd-ntp;
ntn = SpY; nfp = Nn-ntn;
Y=1;
run;

/*Apply the NLMIXED procedure to fit the equation(3)in Section 2 */
proc nlmixed data=tnmeta fd df=1000 gtol=1e-10;
parms eta0 = 2.1 alpha0 = 1.2 beta0 = 1 sigpi = 1 sigse = 1  sigsp = 1 fZ = 0 fZ1 = 0 fZ2 = 0;
lsei = alpha0 + muse ;
lspi = beta0  + musp ;
lppi = eta0   + mupi ;
Sei = 1/(1+exp(-lsei));
Spi = 1/(1+exp(-lspi));
ppi = 1/(1+exp(-lppi));
RhoSeSp = (exp(2*fZ)-1)/(exp(2*fZ)+1);
RhoSePi = (exp(2*fZ1)-1)/(exp(2*fZ1)+1);
RhoSpPi = (exp(2*fZ2)-1)/(exp(2*fZ2)+1);
g1 =  ntp*log(Sei)+nfn*(log(1-Sei))+ntn*log(Spi)+nfp*log(1-Spi);
g2 =  ntp * (log(ppi) + log(Sei)) + nfp * (log(1-ppi) + log(1-Spi)) + nfn * (log(ppi) + log(1-Sei)) + ntn * (log(1-ppi) + log(Spi ));
logL=(design=0)*g1+(design=1)*g2; /*full log-likelihood*/
model Y ~ general(logL);
random muse musp mupi~normal([0, 0, 0],
                                                              [exp(2*sigse),
                                                               RhoSeSp*exp(sigse+sigsp), exp(2*sigsp),
                                                               RhoSePi*exp(sigse+sigpi), RhoSpPi*exp(sigsp+sigpi), exp(2*sigpi)])
subject=id;
estimate "sigse" exp(sigse);
estimate "sigsp" exp(sigsp);
estimate "sigpi" exp(sigpi);
estimate "Se" 1/(1+exp(-alpha0));
estimate "Sp" 1/(1+exp(-beta0));
estimate "Dise Prev" 1/(1+exp(-eta0));
estimate "PPV" exp(eta0+alpha0)*(1+exp(beta0))/(exp(eta0+alpha0)*(1+exp(beta0))+(1+exp(alpha0)));
estimate "NPV" exp(beta0)*(1+exp(alpha0))/(exp(beta0)*(1+exp(alpha0))+exp(eta0)*(1+exp(beta0)));
estimate "logitSe" alpha0;
estimate "logitSp" beta0;
estimate "logitDise Prev" eta0;
estimate "logitPPV" log( exp(eta0+alpha0)*(1+exp(beta0))/(exp(eta0+alpha0)*(1+exp(beta0))+(1+exp(alpha0))) ) -
                    log( 1 - exp(eta0+alpha0)*(1+exp(beta0))/(exp(eta0+alpha0)*(1+exp(beta0))+(1+exp(alpha0))) );
estimate "logitNPV" log( exp(beta0)*(1+exp(alpha0))/(exp(beta0)*(1+exp(alpha0))+exp(eta0)*(1+exp(beta0))) )-
                    log( 1 - exp(beta0)*(1+exp(alpha0))/(exp(beta0)*(1+exp(alpha0))+exp(eta0)*(1+exp(beta0))) );
ods output ParameterEstimates=IaParaEst0 AdditionalEstimates=IaAddEst0;
run;
```