Supplementary Material

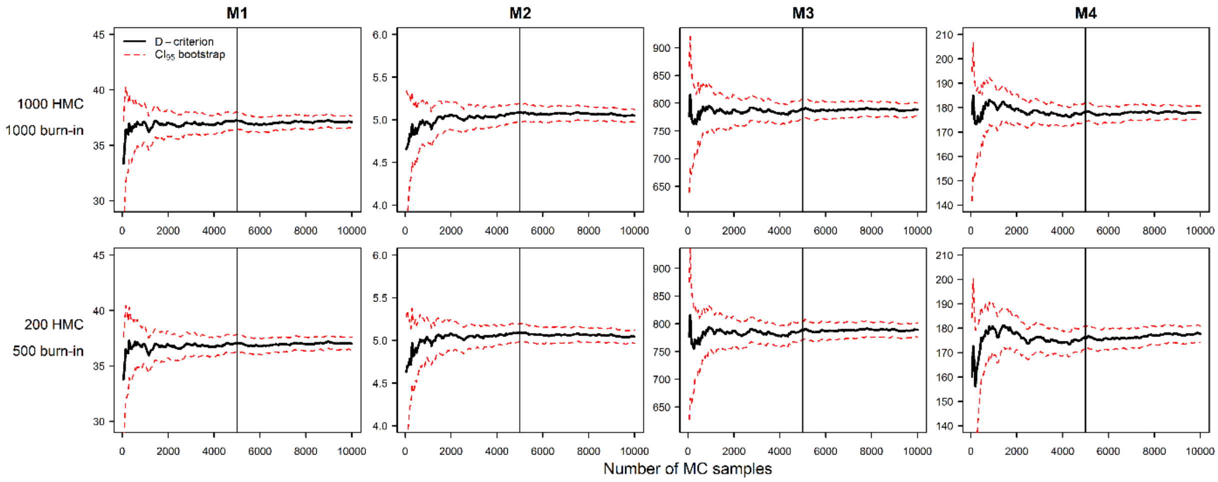

Figure S1. Convergence plots of D-criterion with a non-optimized design. The D-criterion is plotted in black as a function of the number of Monte Carlo samples, with the equispaced design , for each model M1 to M4 by column. For the computation of the Fisher information matrix, two different algorithm settings are displayed by row (1000 Hamiltonian Monte-Carlo (HMC) samples with 1000 burn-in on the left or 200 HMC with 500 burn-in on the right). The red dotted lines represent the 2.5th and the 97.5th percentiles of the D-optimality values using bootstrap.

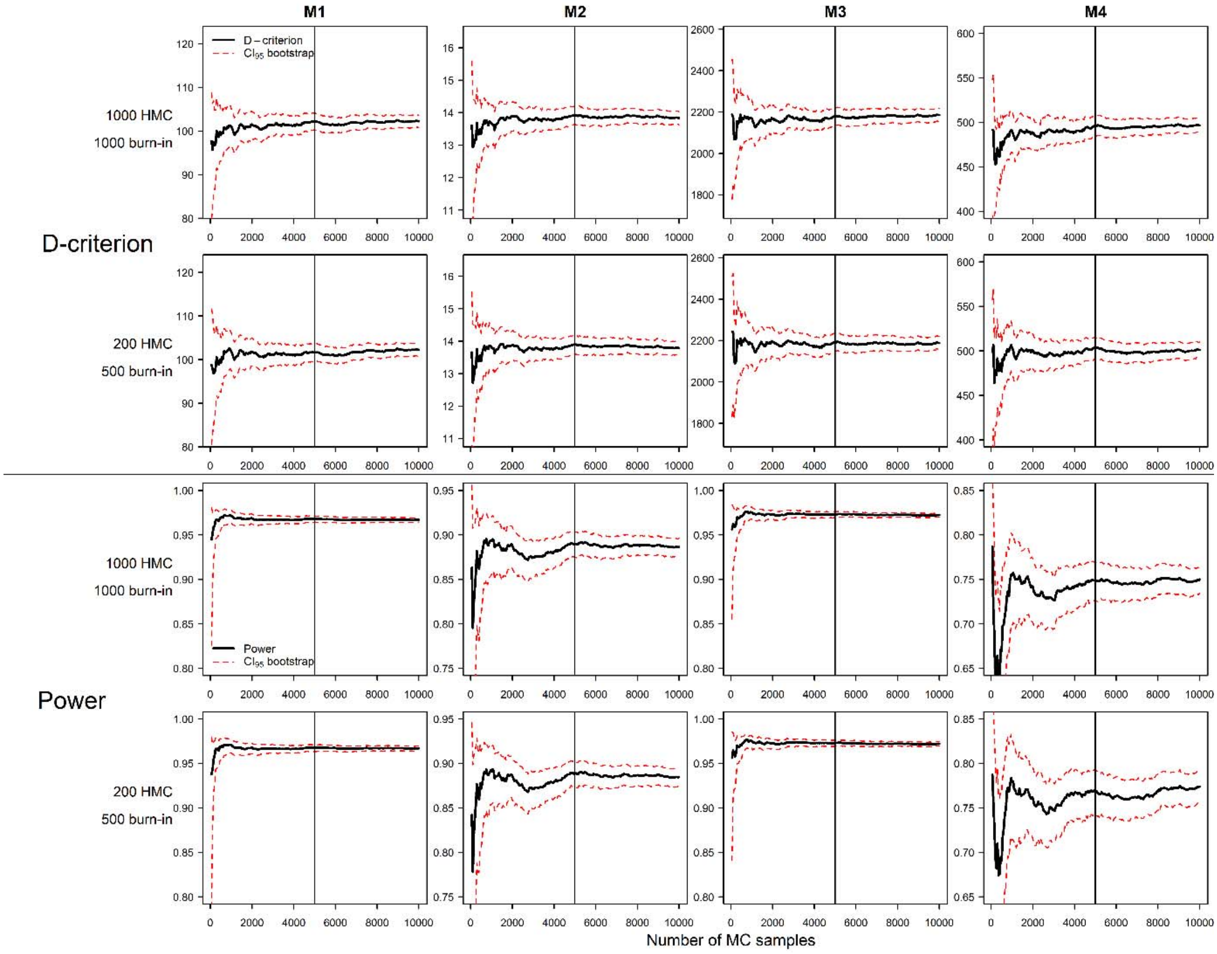

Figure S2. Convergence plots of D-criterion and power with the robust design. For each model M1 to M4 by column, the D-criterion on the top part and the power on the bottom part, are plotted in black as a function of the number of Monte Carlo samples with the robust design . Different algorithm settings for the computation of the Fisher information matrix are represented (1000 Hamiltonian Monte-Carlo (HMC) samples and 1000 burn-in on the first row of each part or 200 HMC and 500 burn-in on the second row of each part), The red dotted lines represent the 2.5th and the 97.5th percentiles of the bootstrap values

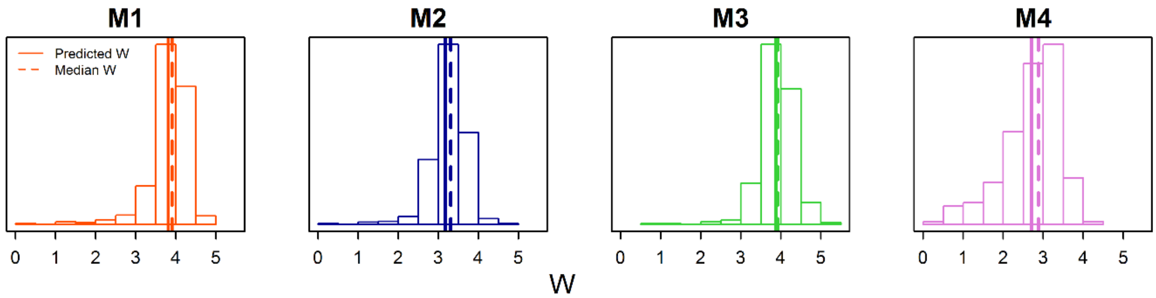

Figure S3. Distribution of observed Wald test statistic with the robust design. For each model M1 to M4, the distribution of the 500 observed Wald test statistic W is represented as histograms. For each model, the solid line is the FIM predicted W and the dashed line is the median of observed W.

Table S1. Observed power of the Wald test without bias on with the robust design.

	M1	**M2**	**M3**	**M4**
FIM predicted power	0.968	0.889	0.973	0.77
CTS observed power	0.988	0.988	0.996	0.86
CTS observed power using simulated	0.976	0.914	0.992	0.746

FIM predicted power are obtained using the true value of (5) and the SE() calculated from FIM evaluation. CTS observed power are obtained using estimated and their SE() as given by the SAEM algorithm. CTS observed power using simulated are obtained using the true value of (5) and SE() as given by the SAEM algorithm.